In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 15-1066V

Filed: May 18, 2020

KATHY CASTANEDA, *on behalf of* N.A.C., a minor child, Petitioner, v. SECRETARY OF HEALTH AND HUMAN SERVICES, Respondent.	PUBLISHED Dismissal; Pentacel, MMR, Prevnar 13 Vaccines; Pediatric Acute Onset Neuropsychiatric Syndrome (PANS); Insufficient Proof of Causation

Andrew D. Downing, Van Cott & Talamante, PLLC, Phoenix, AZ, for Petitioner.
Daniel A. Principato, U.S. Department of Justice, Washington, DC, for Respondent.

DECISION DENYING ENTITLEMENT[1]

Oler, Special Master:

On September 25, 2015, Petitioner Kathy Castaneda, on behalf of her son, N.A.C., filed a petition seeking compensation under the National Vaccine Injury Compensation Program (the "Vaccine Program").[2] Pet., ECF No. 1. Petitioner subsequently filed an amended petition on November 29, 2016 alleging that N.A.C. suffered pediatric acute-onset neuropsychiatric syndrome

[1] This decision will be posted on the United States Court of Federal Claims' website, in accordance with the E-Government Act of 2002, 44 U.S.C. § 3501 (2012). **This means the Decision will be available to anyone with access to the internet**. As provided in 42 U.S.C. § 300aa-12(d)(4)(B), however, the parties may object to the decision's inclusion of certain kinds of confidential information. To do so, each party may, within 14 days, request redaction "of any information furnished by that party: (1) that is a trade secret or commercial or financial in substance and is privileged or confidential; or (2) that includes medical files or similar files, the disclosure of which would constitute a clearly unwarranted invasion of privacy." Vaccine Rule 18(b). Otherwise, this decision will be available to the public in its present form. *Id.*

[2] The Vaccine Program comprises Part 2 of the National Childhood Vaccine Injury Act of 1986, Pub. L. No. 99-660, 100 Stat. 3758, codified as amended at 42 U.S.C. §§ 300aa-10 through 34 (2012) ("Vaccine Act" or "the Act"). Individual section references hereafter will be to § 300aa of the Act (but will omit that statutory prefix).

(PANS), "an overlap of symptoms of OCD, Tourette's syndrome, ADHD, and bipolar disorder," as a result of the Pentacel, MMR, Hepatitis A,[3] and Prevnar 13 vaccinations N.A.C. received on September 26, 2012. Am. Pet., ECF No. 32.

Upon review of the evidence submitted in this case, I find that Petitioner has failed to carry her burden showing that she is entitled to compensation under the Vaccine Act. Petitioner has failed to show that the condition from which N.A.C. suffered was caused by his vaccinations. As such, entitlement to compensation is denied and the petition is dismissed.

I. Procedural History

Petitioner filed her petition[4] on September 25, 2015. ECF No. 1. She filed medical records on November 20, 2015 (Exs. 1, 2, 3), December 9, 2015 (Exs. 4, 5), February 1, 2016 (Ex. 6), February 17, 2016 (Ex. 7), March 14, 2016 (Ex. 8), and November 8, 2018 (Ex. 47).

Respondent filed a Rule 4(c) Report on May 31, 2016 presenting his analysis of Petitioner's claims and recommending that compensation be denied. Resp't's Rep., ECF No. 23-1. Petitioner subsequently filed an amended petition on November 29, 2016. ECF No. 32.

On March 2, 2017, Petitioner filed Dr. Kiki Chang's expert report along with his curriculum vitae ("CV"). Exs. 14, 15; ECF Nos. 41-42. Petitioner filed all of the medical literature cited by Dr. Chang on March 21, 2017. Exs. 16-34, ECF Nos. 44-45.

On June 14, 2017, Respondent filed an expert report by Dr. Donald Gilbert, his CV, and all of the cited medical literature. Exs. A, A1-A11, B; ECF Nos. 47-48.

Petitioner filed an updated CV for Dr. Chang as well as additional medical literature on September 5, 2018. Exs. 35-37, ECF Nos. 54-55. Petitioner filed her prehearing brief on September 6, 2018. ECF No. 56. Respondent's submission followed on September 23, 2018. ECF No. 57.

Between September 25 and September 27, 2018, Petitioner filed additional medical and school records. Exs. 38-40, ECF Nos. 61-63.

I held an entitlement hearing on October 4 and October 5, 2018. After the hearing, Petitioner filed additional medical literature on October 26, 2018. Exs. 43-46, ECF No. 72. The two volumes of the hearing transcript were entered on November 5, 2018. ECF Nos. 75-76. On November 7, 2018, Respondent filed a compact disc containing videos that were played during the entitlement hearing. Exs. D, E, F. Petitioner filed additional medical records on November 8, 2018. Ex. 47, ECF No. 78.

[3] The vaccination record indicates that N.A.C. did not receive his Hepatitis A vaccine on September 26, 2012. *See* Ex. 1.

[4] This case was initially assigned to now-retired Special Master Millman (ECF No. 4) and re-assigned to my docket on January 16, 2018 (ECF No. 51).

On December 18, 2018, the parties filed a joint status report indicating that "the record is complete." ECF No. 79. I issued a scheduling order setting deadlines by which the parties were to submit their respective post-hearing briefs. *See* Non-PDF Order of December 19, 2018. Petitioner filed her brief on February 18, 2019 (ECF No. 80) and Respondent filed his brief on May 17, 2019 (ECF No. 84).

On September 10, 2019, I issued an order asking each expert to answer several questions. ECF No. 97. Petitioner filed a response from Dr. Chang on November 15, 2019. Ex. 49, ECF No. 99. Respondent filed a response from Dr. Gilbert on December 10, 2019. Ex. C, ECF No. 102. Petitioner filed a response to Dr. Gilbert's supplemental report on December 19, 2019. ECF No. 103. Respondent re-filed Petitioner's Facebook page on February 26, 2020. Ex. G. This matter is now ripe for a decision.

II. Medical Records

A. Petitioner's Health Prior to the Allegedly Causal Vaccination

N.A.C. was born on October 9, 2007. He presented to the pediatrician for well-child visits at two months (Ex. 47 at 18, 50), four months (Ex. 47 at 48), six months (Ex. 47 at 13, 60), 12 months (reference to this visit at Ex. 47 at 3), and 18 months (Ex. 47 at 65). No records of any additional well-child visits were filed in this case.[5]

N.A.C. was treated for various complaints prior to his September 26, 2012 vaccinations. *See* Ex. 4 at 122, 124, 131 (ER visit on July 3, 2010 at Washington County Hospital ("WCH") for fever, diagnosed with otitis media); *id*. at 112-13, 118 (ER visit on July 4, 2010 at WCH for rash); Ex. 3 at 5-7 (visit at Martin General Hospital on July 5, 2010 for chickenpox); Ex. 4 at 102 (ER visit at WCH February 5, 2011 for earache); *id*. at 93, 98 (ER visit at WCH on May 28, 2011 for laceration on right foot sustained after a fall); *id*. at 83 (ER visit at WCH on February 22, 2012 for cough, fever, and vomiting); *id*. at 73, 76 (ER visit at WCH on April 19, 2012 due to cutting finger with a knife); *id*. at 61, 63 (N.A.C. burned his left hand (palm) by grabbing something plastic that melted and subsequently went to the zoo and fell on his hand, he had an ER visit at WCH on May 29, 2012); Ex. 7 at 2, 3 (visit with primary care physician on May 31, 2012 that notes N.A.C.'s

[5] I held a status conference with the parties on September 25, 2018 and requested that Petitioner file all of N.A.C.'s well-child visits that pre-date his September 26, 2012 vaccinations. ECF No. 64. During the hearing, when asked about well visits, Petitioner testified that the well visits are "from birth on up to like maybe two, three. And that has all his baby checkups and birth weights, all of that from birth on up." Tr. at 87. At the hearing, I reiterated my request that Petitioner file medical records that specifically contain these well visits, as none had been filed up to this point. Tr. at 417. Petitioner filed additional medical records after the hearing (Ex. 47), but these records did not include any well visits after 18 months. In a supplemental affidavit, Petitioner stated that "N.C. was a healthy child without any complaints, so I did not take him in for either a 24-month or 36-months well-child checkup." Ex. 48. Respondent's expert, Dr. Gilbert describes the pre-vaccination evidence in this case as "a complete absence of standard medical records from […] 2 year and 3 year well child visits." Ex. C at 3. I agree with this assessment and note that the absence of such records makes analysis of the issues in this case more difficult.

second degree burn on left hand); *id*. at 4-5 (visit with primary care physician on June 7, 2012 for follow up regarding left hand burn).

B. Petitioner's Health after the Allegedly Causal Vaccination

On September 26, 2012, N.A.C. received MMR, Prevnar 13, and Pentacel vaccinations.[6] *See generally* Ex. 1.

On October 9, 2012, N.A.C. was admitted to Vidant Medical Center with complaints of behavioral problems, which included a twitch, stutter, and increased crying. Ex. 5 at 1, 2. The "behavior problem" was described as new, starting "in the past few days." *Id*. at 3. His mother reported that N.A.C. "has always been an irritable child but has been worse over the past few weeks. He has been fussy, crying more frequently, and misbehaving." *Id*. at 2. He was reported to be walking strangely by taking one or two steps and then shuffling. *Id*. His mother also reported that N.A.C. had "been leaning his head right, then left, then saying 'stop'" and had been doing so repeatedly. *Id*. N.A.C. cried during his examination but stopped crying in order to answer questions. *Id*. He denied pain and denied headache. *Id*. He did not have a fever. *Id*. at 3. His physical examination was generally normal, however, during his psychiatric exam he was noted to appear anxious and agitated. *Id*. at 4. The doctor indicated that N.A.C.'s behavior problems "seem to be an exacerbation of some ongoing behavior problems" and noted his mother's concerns that N.A.C.'s symptoms may be tics. *Id*. N.A.C.'s head CT results were normal. *Id*. at 5. The differential diagnoses were "ODD [Oppositional Defiant Disorder], tic/Tourettes, ongoing chronic behavior problems, [and] intracranial process". *Id*. at 4. The doctor provided Petitioner with the contact information for child psychiatry. *Id*. at 5.

The medical record of N.A.C.'s October 11, 2012 visit notes that patient "complained of unusual behavior." Ex. 8 at 3. N.A.C.'s medical record reports that on October 12, 2012, N.A.C. was seen for a follow up and that his "behavior seems to [be getting] worse." Ex. 8 at 2. N.A.C.'s temperature was listed as 97.9˚. *Id*.

On October 15, 2012, N.A.C. saw Dr. Ingrid Loma-Miller (a neurologist) for his abnormal involuntary movements. Ex. 2 at 10. Petitioner informed the doctor that on September 27th, about one or two days after his MMR vaccination, N.A.C. "started having episodes of abnormal movements consisting of neck flexion, shoulder shrugging and throat clearing episodes." *Id*. While N.A.C. is aware of his episodes, he is unable to stop. *Id*. N.A.C. also had episodes "where he would bang his head against the wall." *Id*. His episodes were described to include obsessive behaviors, which included repeating actions three times. *Id*. Petitioner expressed her concerns that his episodes are "related to the vaccine that he got." *Id*. During the examination, N.A.C. made good eye contact but was noted to be uncooperative and refused to answer certain questions. *Id*. at 11. He was able to name objects correctly when asked by Petitioner but only limitedly. *Id*.

[6] Petitioner stated during testimony and in a letter to the Nursing Board (Ex. 39) that N.A.C. received four vaccinations on the date in question. However, N.A.C.'s vaccination record shows that Petitioner received only three vaccinations as listed above. Ex. 1. In the letter to the Nursing Board, Petitioner represented that the record was incorrect and N.A.C. received a fourth vaccination (Varicella), that was deleted from N.A.C.'s record.

Overall, his neurologic exam appeared to be normal. *Id.* Dr. Loma-Miller assessed N.A.C. with "new-onset [of] abnormal movements, which appear to be tic-like in type." *Id.* The record notes that Dr. Loma-Miller "explained to the mother that [she] [does] not think that [N.A.C.'s] abnormal movements are related to the vaccines" and that "[t]here [were] no specific data in the medical literature to support such concerns." *Id.* Regarding N.A.C.'s tics, Dr. Loma-Miller wondered if N.A.C. had a tic disorder that could possibly be Tourette syndrome due to N.A.C.'s motor and vocal tics. *Id.* She noted that N.A.C. had yet to meet the criteria for Tourette at such time due to the fact symptoms had been occurring for less than one month. *Id.* Dr. Loma-Miller also explained to Petitioner that OCD has been observed alongside tic disorders, and N.A.C. may exhibit symptoms of OCD behavior along with his tic disorder. *Id.*

N.A.C. saw his primary care physician on October 18, 2012 and the record notes, "mother states wants [sic] blood test." Ex. 7 at 16. The record also indicates, "abn[ormal] behavior r/o tic." *Id.* at 17.

N.A.C. presented to Dr. Loma-Miller for a follow-up visit on November 9, 2012 in order to discuss his EEG results. Ex. 2 at 8; *see also* Ex. 2 at 12. The record indicates that N.A.C. continued to have episodes of abnormal movement since his previous visit. Ex. 2 at 8. Petitioner reported to Dr. Loma-Miller that N.A.C. has also been getting very moody and aggressive. *Id.* Dr. Loma-Miller noted that Petitioner had done research on Tourette syndrome and reported that N.A.C. was exhibiting many of the symptoms, including "facial grimacing, shoulder shrugging, sniffing, throat clearing and squeaking." *Id.* Petitioner also reported that N.A.C. had been acting impulsively and had several compulsions, such as "rechecking things over and over again, smelling things, touching things…. He has to do 3 of everything." *Id.* Petitioner told Dr. Loma-Miller that the Tenex had not improved the tics and that his behavior was more concerning at that time, adding that he was sleeping well. *Id.* Neurologic examination was normal, and N.A.C. was noted to have good eye contact, but was fidgety and hyperactive. *Id.* at 9. His EEG was normal. *Id.* The doctor also noted his blood work, which showed: ANA was negative; his lead was less than 5; his "[c]omplete metabolic panel [was] normal except for mildly elevated AST of 39 and sodium 139"; and his "CBC was significant for decreased hemoglobin and hematocrit of 12.4/35 with MCV low at 78." *Id.* Dr. Loma-Miller's assessment noted that N.A.C. was neurologically stable and had abnormal involuntary movements, "which appear to be more tic behavior and consistent with Tourette syndrome." *Id.* Dr. Loma-Miller directed that N.A.C. to stop taking Tenex[7] and try Clonidine[8] for his behavioral issues. *Id.* Lastly, the doctor provided a referral for behavioral therapy and psychology. *Id.*

[7] Tenex is the trademark for a preparation of guanfacine hydrochloride. DORLAND'S ILLUSTRATED MEDICAL DICTIONARY (33rd ed. 2020) at 1853 (hereinafter "Dorland's"). Guanfacine hydrochloride is "an α_2-adrenergic agonist that stimulates the α_2-adrenergic receptors of the central nervous system, resulting in reduction of sympathetic overflow to the heart and peripheral vascular system, used as an antihypertensive, administered orally." *Id.* at 801.

[8] Clonidine is "an α_2-adrenergic agonist-antagonist … administered orally or transdermally as an antihypertensive." Dorland's at 368. The clonidine was to be given at 0.1mg at night and could be scaled up to 0.1mg twice per day if needed. Ex. 2 at 9.

N.A.C. saw Dr. Loma-Miller on March 11, 2013 for a follow-up visit regarding his tic disorder. Ex. 2 at 7. Petitioner reported that Clonidine was helpful, but not consistently. *Id.* Petitioner was not only concerned with N.A.C.'s tic disorder but also his behavior, reporting that he "gets very easily upset, moody, and angry." *Id.* Petitioner recalled for Dr. Loma-Miller that when N.A.C. "gets upset, he starts jumping. He also gets very upset and cries for no reason, very defiant." *Id.* Dr. Loma-Miller noted that N.A.C. had yet to visit psychology. *Id.* The record further indicates that N.A.C. has "OCD where he has to have a certain pattern of doing things." *Id.* The record describes his pattern of closing the bathroom door and rotating store products to face forward. *Id.* Petitioner reported that if N.A.C. is unable to conduct his same routine, he becomes very upset. *Id.* Regarding N.A.C.'s development, Petitioner reported that he has been learning new things and now knows his shapes. *Id.* Physical examination was normal, although the doctor noted that N.A.C. was still shy and not making eye contact. *Id.* at 7. Neurological examination was normal, although the doctor noted that N.A.C. was "very fidgety like before, very hyperactive." *Id.* Dr. Loma-Miller noted in his assessment that N.A.C. had a history of tic disorder, and that he meets the criteria for Tourette syndrome. *Id.* Dr. Loma-Miller, again, referred N.A.C. to psychology, and she explained to Petitioner the importance of scheduling this appointment in order to assist N.A.C. with his behavioral problems. *Id.*

On August 27, 2013, N.A.C. saw Dr. Loma-Miller at Children's Hospital's neurology office. Ex. 2 at 4. Petitioner reported that he "has been doing the same." *Id.* She further reported that "[f]ather did not want to go up on his dose … therefore he only takes clonidine, one tablet at night." *Id.* Petitioner stated that the Clonidine did not change N.A.C.'s tics and that he "still has some eye blinking." *Id.* N.A.C. was noted to be "constantly bothered." *Id.* Petitioner denied concerns for headaches, seizure activity, focal weakness, numbness or tingling. *Id.* Dr. Loma-Miller noted that Petitioner expressed interest in having N.A.C. evaluated for autism. *Id.* N.A.C. was uncooperative during physical examination and did not respond to any questions. *Id.* at 5. He was able to follow "one-step commands" but had difficulty completing complex tasks. *Id.* Neurologic examination was normal. *Id.* Dr. Loma-Miller's assessment noted N.A.C.'s history of Tourette syndrome and Dr. Loma-Miller "agree[d] with [N.A.C.'s] mom that he may be in the spectrum of autism, but however, it is not clear cut…." *Id.* Dr. Loma-Miller referred N.A.C. to Developmental Pediatrics for autism evaluation, directed that N.A.C. continue taking Clonidine, and recommended that N.A.C. take Miralax for bowel incontinence and constipation. *Id.* Dr. Loma-Miller again encouraged Petitioner to have N.A.C. follow up with psychology for behavioral therapy and treatment. *Id.*

On August 30, 2013, N.A.C. saw his primary care physician for a kindergarten physical. Ex. 7 at 14.

N.A.C. had an ER visit at WCH on January 16, 2014 for fever and cough. Ex. 4 at 34-35. His history of Tourette syndrome was noted. *Id.* at 35. Lab results revealed that N.A.C. tested positive for influenza A protein antigen. *Id.* at 38.

On May 7, 2014, N.A.C. had an ER visit at WCH for an itchy rash that he had on his buttocks for the past three days. Ex. 4 at 22, 25. The medical record notes that he is taking Clonidine. *Id.* at 23.

N.A.C. had an ER visit at WCH on June 2, 2014 for a splinter in his foot. Ex. 4 at 8-9. His history of Tourette syndrome is also noted in the medical records. *Id*. at 12, 20.

On August 11, 2014, N.A.C. was seen at the Children's Hospital of The King's Daughters ("Children's Hospital") pediatric neurology office by Dr. Matthew S. Warren. Ex. 2 at 2. The record notes his routine visits with the office's neurologist, Dr. Loma-Miller, as well as N.A.C.'s history of vocal and motor tics and diagnosis of Tourette syndrome. *Id.* The record notes that N.A.C.'s tics wax and wane. *Id*. The record indicates a concern that N.A.C. fits the autism spectrum and notes his family history is positive for autism but that there are no psychiatric issues in the family. *Id*. Physical and neurologic examinations were normal, however, the doctor noted that N.A.C. is uncooperative during examination and that he refuses to walk on his toes; N.A.C. had temper tantrums in the office. *Id*. at 3. The doctor's impression remained Tourette syndrome with comorbid ODD. The doctor noted Dr. Loma-Miller's encouragement that N.A.C. see a psychologist, which had yet to occur, however, according to Dr. Warren, N.A.C. "definitely needs a psychological evaluation." *Id*.

A medical record that reflects an admit date of September 18, 2014 reports N.A.C.'s hematology results. Ex. 7 at 11. The record notes that N.A.C. has a history of "anemia – CBC". *Id*. at 12. The record also notes that N.A.C. had "ice cold" and "white (pale) color" hands for the past two days as well as "dark colors under eyes." *Id*. at 13.

A medical record dated May 29, 2015 notes "refer to psyc" and "clonidine". Ex. 7 at 9. N.A.C.'s history of Tourette syndrome, Attention-Deficit/Hyperactivity Disorder ("ADHD"), Obsessive-Compulsive Disorder ("OCD"), and ODD is noted in the medical record. *Id.* at 10.

On July 2, 2015, N.A.C. saw his primary care physician for prescription refills. Ex. 7 at 7. The record notes "tic", "ADHD", and "f/u psyc" as well as "clonidine". *Id*. at 8.

N.A.C. visited Martin General Hospital on July 30, 2015 for left ear pain that began two days prior to his visit. Ex. 3 at 1-2. The medical record notes a history of Tourette syndrome. *Id*. at 2. N.A.C. was diagnosed with otitis externa. *Id*. at 3.

No other medical records filed were pertinent to the issues to be addressed in this case.

III. School Records

Petitioner filed records from evaluations N.A.C. received in a school setting. *See* Ex. 40. Kimberly Page Reel, a licensed psychological associate at N.A.C.'s school, administered several tests, which included the Childhood Autism Rating Scale (CARS-2) and the Gilliam Autism Rating Scale (GARS-3). With respect to the GARS-3, both Petitioner and N.A.C.'s teacher provided responses to questions indicating, in the opinion of the assessor that "it is very likely that [N.A.C.] demonstrates behaviors consistent with an Autism Spectrum Disorder." Ex. 40 at 55. The results of the CARS-2 were not as pronounced; the general impression of N.A.C.'s teacher "is that [N.A.C.] displays a mild degree of symptoms similar to a child with an Autism Spectrum Disorder." *Id.* at 54. In summary, Ms. Reel indicated that N.A.C. "may be autistic." *Id.* at 55.

IV. Affidavits and Fact Testimony

A. Affidavits

Petitioner reported that "[i]n the days following" N.A.C.'s vaccinations, she "started noticing odd things with N.A.C."[9] *See* Statement of Kathy Castaneda, Ex. 13 at 2. Petitioner stated that N.A.C.'s odd actions became a daily occurrence, and she and her husband were unable to determine what was going on; they attributed N.A.C.'s actions to "just being a kid, because kids do weird things." *Id*. Their concerns continued to grow as N.A.C. told them that he could not stop his behavior, even though he got in trouble. *Id*.

On October 9, 2012, N.A.C. was admitted to Vidant Medical Center with complaints of behavioral problems, which included a twitch, stutter, and increased crying. Ex. 5 at 1, 2. Petitioner explained that about two or three days prior to his October 9, 2012 admission at Vidant Medical Center, "N.A.C.'s symptoms had worsened." Ex. 13 at 2. She stated that he began "stuttering really badly to the point that he could barely say anything" and that he "started banging his head into things…and would repeat the word 'stop' as he banged his head." *Id*. N.A.C. would continue banging his head until he cried, and he would inform Petitioner that he could not stop. *Id*.

Petitioner noted that while at Vidant Medical Center she asked the doctor whether vaccines could be the cause of N.A.C.'s problems, and that "[t]he doctor told us that the vaccines could have possibly caused this." Ex. 13 at 3. The medical record does not reflect this conversation. *See generally* Ex. 5.

On October 11, 2012, Petitioner took N.A.C. to see Dr. Myung Kil Jeon, at Plymouth Primary Care. Ex. 13 at 3. The doctor said that N.A.C. was having tics and involuntary body movements. *Id.* Petitioner wrote that she asked if the vaccines could have caused this, and according to Petitioner, the doctor said yes. *Id.* The medical record does not reflect this conversation. *See generally* Ex. 8.

On October 15, 2012, Petitioner and her husband took N.A.C. to a neurology appointment. Ex. 13 at 3. According to Petitioner, the neurologist informed her that Tourette syndrome could

[9] Petitioner provided the following examples:

> …when he walked, he would walk a couple of steps, stop suddenly, and then repeat this process. He would move his head to his shoulder so that the side of his head touched his shoulder two or three times. His head would go down and his shoulder would shrug up to meet his head, and then he would quickly do the same thing on the opposite side….[he] also started spitting on his shoulder….[he] began to copy what [her] husband and [she] would say….[he] started doing things in threes; for example, he would pick up or set down his cup three times (same with his toys, eating utensils, crayons, or anything he could pick up). He would flush the toilet three times, turn lights on and off three times, and had to go through any doorway three times.

Ex. 13 at 2.

not be diagnosed until February 2013. *Id.* at 3-4. When Petitioner asked if the vaccines could have caused N.A.C.'s condition, the doctor "was quick to say no" because "the government frowns on doctors who say injuries occur from vaccines." *Id.* at 4.

Petitioner also stated that she did not take N.A.C. to either a 24-month or 36-month well-child checkup because he was a "healthy child". Ex. 48 at 1.

B. Fact Testimony

Petitioner testified at the October 4, 2018 hearing. She described N.A.C. as a playful little boy who loved being outdoors. Tr. at 10. Petitioner also testified that N.A.C. met all of his milestones and experienced no obsessive-compulsive tendencies or tics prior to the allegedly causal vaccinations. *Id.* at 10, 12. Petitioner stated that on September 26, 2012, N.A.C. was supposed to receive a total of five vaccinations but had gotten chicken pox from his brother's live virus varicella vaccination in 2009 and didn't need the varicella vaccination, therefore N.A.C. only received four vaccinations. *Id.* at 14-15.

Petitioner stated that on the next day, approximately 30 hours after vaccination, she was holding hands with N.A.C. and he abruptly stopped walking, stepped in place three or four times, continued walking a few steps, and stepped in place again. This cycle repeated. Tr. at 15-16. N.A.C. would also move his head from shoulder to shoulder repeatedly. *Id.* at 16. Another tic that N.A.C. developed was spitting on his own shoulder, covering his shirt with saliva. *Id.* Petitioner recalled an incident where N.A.C.'s father reprimanded N.A.C. for spitting on his shirt and on the couch and told N.A.C. to stop spitting. *Id.* N.A.C. said he could not stop spitting and began crying and telling himself to stop. *Id.* at 16-17.

Petitioner described other changes in N.A.C., which included N.A.C. having aggressive fits. Tr. at 17. N.A.C. would throw toys or small objects and would kick, bruising his parents and siblings. *Id.* at 17, 36, 45-46. N.A.C. would also flush the toilet three times, pick up and set things down multiple times, flip the light switch on and off, and jump in the same place repeatedly. *Id.* at 18, 47. Petitioner bought N.A.C. a trampoline because N.A.C. wanted to jump on a springy surface and ruined their couch by his jumping. *Id.* at 47-48. Petitioner also noted that N.A.C. became less social and got angry at himself for not being able to stop his tics. *Id.* at 18, 42-43. N.A.C. would frequently bang his head against various surfaces. *Id.* at 18, 24.

Petitioner testified that neither N.A.C.'s sibling nor half-siblings have any neuropsychiatric behavioral issues. Tr. at 60. None of N.A.C.'s extended family members have Tourette syndrome or tic-based behaviors, though Petitioner's brother, N.A.C.'s uncle, has ADHD. *Id.* at 69-70.

V. Expert Opinions

A. Dr. Kiki Chang

Petitioner filed one expert report and one supplemental report from Dr. Kiki Chang; Dr. Chang also testified at the hearing. *See* Expert Report, filed as Ex. 14, hereinafter "Chang Rep." and Supplemental Expert Report, filed as Ex. 49, hereinafter "Chang Supplemental Rep.".

1. Qualifications

Dr. Chang attended Princeton University and graduated in 1988 with a degree in molecular biology. *See* Chang CV at 1, filed as Ex. 15 (ECF No. 42) ("Chang CV"). He then attended Tufts Medical School, graduating in 1993. *Id.* Dr. Chang completed his residency at the University of Cincinnati in general psychiatry. *Id.* After his general residency, Dr. Chang completed a three-year combined research and clinical fellowship in child and adolescent psychiatry at Stanford University. *Id.* In 1999, Dr. Chang was appointed as an assistant professor of psychiatry and behavioral sciences at Stanford University. Tr. at 99. During his time at Stanford, Dr. Chang was on the faculty at Stanford University Hospital and Stanford's Children's Hospital. *Id.* at 100. He is currently licensed in California. Chang CV at 1.

After approximately 18 years at Stanford, Dr. Chang opened his own practice. Tr. at 98-99. He currently sees patients two to three days per week. *Id.* at 99. Dr. Chang treats children, adolescents, and adults with complex psychiatric and neuropsychiatric illnesses. *Id.* He treats patients with bipolar disorder, serious mood disorders, anxiety disorders, pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection ("PANDAS"), and PANS. *Id.* Dr. Chang spends approximately 70% of his time in clinical practice. *Id.* at 97. Approximately 30% of his time is devoted to consultations and speaking about various psychiatric illnesses. *Id.* Dr. Chang is a member of the American Association of Child and Adolescent Psychiatry and the American College of Neuropsychopharmacology. Chang CV at 1. Dr. Chang has published numerous medical journal articles and has participated as a journal referee, peer-reviewing journal articles. Tr. at 100. I recognized Dr. Chang as an expert in the areas of Pediatric and Adolescent Psychiatry, and Neuropsychiatric Illness. *Id.* at 106.

2. Expert Testimony

In his report and at the hearing, Dr. Chang opined that N.A.C. developed PANS as a result of the vaccinations he received on September 26, 2012. Chang Rep. at 4; Tr. at 197.

In 2012, Dr. Chang formed Stanford University's PANS clinic. Tr. at 103. In 2013, Dr. Chang organized the expert consensus meeting for researchers on PANS and PANDAS at Stanford University. *Id.* at 102. At that meeting, experts clarified the clinical criteria for a diagnosis of PANS. *Id.* Dr. Chang estimated that he has seen anywhere from 100 to 200 patients diagnosed with PANS. *Id.* at 104.

Dr. Chang went on to explain that in the 1990s, Dr. Susan Swedo at the National Institutes of Health proposed PANDAS as a diagnosis. Tr. at 106. Dr. Chang explained that this disorder involves an acute onset of OCD along with accompanying symptoms such as "motor tics, behavioral problems, changes in … handwriting, changes in … focus and concentration, extreme aggressiveness, irritability, depression, [and] extreme separation anxiety" that occur after strep infection. *Id.* at 107.

PANS was then established as a diagnosis to address the fact that some children displayed acute onset of various symptoms without clear-cut streptococcal infection. Tr. at 109. Dr. Chang

explained that with respect to acuity of onset, it was agreed at the 2013 meeting that for PANS, onset of comorbid symptoms is between 48 and 72 hours. *Id.* at 111. Dr. Chang further clarified that "what that means is that it had to be going from not noticing any symptoms to noticing significant symptoms within that time as well as the associated symptoms starting to emerge." *Id.* He stated that "it couldn't be something that may have developed gradually over a month or two months or a year." *Id.* Dr. Chang explained the reason for the necessity of acute onset is "to distinguish it between other more typical neuropsychiatric illnesses like OCD and Tourette that tend to have a more gradual onset." *Id.*

Dr. Chang stated that the criteria for PANS differed from PANDAS. Tr at 113. He explained that unlike PANDAS, where the primary criterion is OCD or tics, in PANS the primary criterion must be OCD or an eating restriction. *Id.* Concurrent with that, Dr. Chang stated that a PANS patient must also have at least two of the following symptoms comorbidly: general anxiety, separation anxiety, emotional lability and/or depression, irritability, aggression, oppositional behavior, or behavioral developmental regression, deterioration in school performance, inability to concentrate, becoming hyperactive, hand writing changes, working memory executive function changes, sensory motor abnormalities including motor and vocal tics, and somatic signs and symptoms. *Id.* at 114-15.

Dr. Chang went on to discuss mechanisms for the development of PANDAS and PANS. Tr. at 116. He explained that in both PANDAS and PANS, there is a triggering event, "which is either known or unknown, and because of the triggering event there is an inflammatory reaction that for some reason targets the basal ganglia." *Id.* Dr. Chang stated that the basal ganglia "fine tunes many, if not all, of the brain functions." *Id.* Dr. Chang explained that in both Parkinson's and Tourette syndrome, abnormalities in the basal ganglia have been noted. *Id.* at 117. He stated that several "functional and structural studies done [on] the brain suggest that this area is related to OCD, as well as tics, as well as ADHD symptoms." *Id.* at 118.

Dr. Chang explained that based on his experience, there are two major mechanisms through which PANDAS and PANS may develop. Tr. at 118. The first is an autoimmune mechanism known as molecular mimicry, in which antibodies created against a particular antigen cross-react with brain tissue, including basal ganglia tissue. *Id.* at 119. In other words, parts of an antigen look enough like host brain tissue that the host would make antibodies against it, thinking that might be a defense mechanism, and start attacking its own brain tissue. *Id.* Dr. Chang stated "[s]omehow they would get past the blood-brain barrier, bind to the areas of the brain and trigger inflammatory cascades that would then lead to inflammation and disruption of the area leading to [PANS] symptoms." *Id.*

The second mechanism Dr. Chang described is a general inflammatory reaction driven by cytokine production. Tr. at 120. He explained that such reactions then lead to inflammatory mediators crossing the blood-brain barrier and selectively attacking the basal ganglia. *Id.* Dr. Chang emphasized that he does not know why it would attack the basal ganglia, but that "it's sort of a ripe area due to where it is located in the vasculature." *Id.* Dr. Chang believes that this mechanism is probably "more relevant" for this case. *Id.* He explained that there is some trigger that causes an immune reaction to an inflammatory cascade that selectively hits the basal ganglia and leads to PANS. *Id.* at 121. Dr. Chang stated that this mechanism can be triggered by infection,

by autoimmune conditions, or "it can be triggered by anything that can really cause an inflammatory state, including a vaccination." *Id.* at 122.

Dr. Chang discussed the Parker-Athill article (Parker Athill et al., *Cytokine Correlations in Youth with Tic Disorders*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 25, No. 1, pp. 86-92 (2015), filed as Ex. 25 (hereinafter "Parker-Athill")) as standing for the proposition that inflammatory cytokine production was responsible for tic exacerbation in children with Tourette syndrome or a chronic tic disorder. Tr. at 122-23. He testified that the same pro-inflammatory cytokine tumor necrosis factor alpha is expressed following vaccination. *Id.* at 123. When asked whether the model of cytokine involvement with neuropsychiatric disease is the same for an infection and vaccination, Dr. Chang replied, "it very well could be." *Id.* at 124.

When asked about timing of onset following a known trigger, Dr. Chang stated that onset of symptoms is "usually fairly quick," "within days" of the initial event, "at the most a week." Tr. at 124. Dr. Chang testified that OCD typically has a more gradual onset. *Id.* at 125. He highlighted an article that stated "[a]ll participants exhibited an abrupt onset of OCD and associated neuropsychiatric symptoms in contrast to the gradual onset experienced by children with non-PANS OCD." Tanya K. Murphy et al., *Characterization of the Pediatric Acute-Onset Neuropsychiatric Syndrome Phenotype*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 25, No. 1, pp. 14-25 (2015), filed as Ex. 31.

Dr. Chang went on to compare Ms. Castaneda's testimony regarding her son's symptoms with the clinical criteria for PANS. Under Roman Numeral I, Dr. Chang stated that N.A.C. exhibited both OCD and eating restrictions. Tr. at 130. With respect to Roman Numeral II, Dr. Chang described what he considered to be anxiety, emotional lability, irritability/aggression/oppositional behaviors, behavioral regression, deterioration in school performance, sensory motor abnormalities, and somatic signs and symptoms, all of which he stated N.A.C. exhibited. *Id.* at 132-38. Although the PANS criteria only require at least two symptoms under Roman Numeral II, in his opinion N.A.C. exhibited all seven symptoms. *Id.* at 138. Dr. Chang concluded his analysis by testifying that, as required by Roman Numeral III of the criteria, no other diagnosis better explains N.A.C.'s symptoms. *Id.* at 141.

Dr. Chang testified that Tourette syndrome typically does not present with the comorbidity of symptoms and acuity of onset that was seen in N.A.C.'s condition. Tr. at 141. He stated that Tourette syndrome has a more gradual development from motor tics to vocal tics, followed by comorbidity of OCD and ADHD. *Id.* Dr. Chang testified that Tourette syndrome does not have the same underlying mechanism as PANS. *Id.* When I asked him to clarify, he stated that Tourette syndrome is more commonly associated with a genetic disorder or predisposition. *Id.* at 142.

Dr. Chang went on to discuss the Calaprice article (Calaprice et al., *A Survey of Pediatric Acute-Onset Neuropsychiatric Syndrome Characteristics and Course*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, pp. 1-12 (2017) (filed as Exhibit 16) (This article was double filed as Ex. 16 and Ex. 37). Tr. at 144–47. He explained that this article related to a survey of approximately 700 patients that had been clinically diagnosed with PANS. *Id.* Dr. Chang testified that in this survey, "a significant portion…reported triggering events that have to do with inflammation." *Id.* at 145. About 300 of those surveyed, provided information about events

following vaccination. *Id.* at 146. Dr. Chang testified that of the 300, approximately half reported "that vaccines appeared to precipitate a flare of PANS symptoms." *Id.* In response to my question about whether the article discussed timing between vaccination and flare, Dr. Chang clarified that timing was not indicated. *Id.* at 148.

The final article that Dr. Chang discussed on direct examination was Exhibit 36. Tr. at 150. Douglas L. Leslie, et al., *Temporal Association of Certain Neuropsychiatric Disorders Following Vaccination of Children and Adolescents: A Pilot Case-Control Study*, FRONTIERS IN PSYCHIATRY (2017), filed as Ex. 36 (hereinafter "Leslie"). He testified that this article involved children who presented with neuropsychiatric disorders. *Id.* Using a control group of children with injuries including broken bones and open wounds, the researchers set out to determine what, if any, connection prior vaccinations had to those children with neuropsychiatric disorder. *Id.* at 151. Dr. Chang stated that the study revealed an increased incidence of vaccination three, six, and 12 months prior to a new diagnosis of anorexia nervosa. *Id.* at 152. He stated that anorexia nervosa is often a misdiagnosed food restriction under Roman Numeral I of the PANS criteria. *Id.* Dr. Chang made it clear that this temporal study does not establish causation. *Id.* at 153.

Dr. Chang concluded his direct examination by stating that in his opinion NAC's September 26, 2012 vaccinations triggered his neuropsychiatric disease. Tr. at 154–55. He stated that "it's possible if he never received that vaccination or any vaccinations, it's possible that he never would have developed this." *Id.* at 156–57.

On cross examination, Dr. Chang stated that there is some data, currently not published, to suggest a correlation between PANS and HLA–B5 genotype. Tr. at 158. Dr. Chang is, however, unaware whether N.A.C. possesses HLA–B5. *Id.* at 159. He stated that he is speculating that N.A.C. has some sort of genetic predisposition for PANS. *Id.* Dr. Chang testified that he is not familiar with the exact level of cytokine production following vaccinations. *Id.* at 160. He also testified that he is not aware of any evidence of the permeability of the blood-brain barrier in N.A.C.'s case. *Id.* at 161. Dr. Chang went on to clarify that there is "[n]o way of definitively…seeing if that was actually inflammation going on" in N.A.C.'s case. *Id.* at 162.

Dr. Chang was unable to explain why N.A.C. did not have similar adverse reactions to all of the previous routine vaccinations he had received up until September 2012. Tr. at 165. When asked how one can rule out a diagnosis of autism, Dr. Chang explained that the acuity of onset and the comorbidity of symptoms in N.A.C.'s case do not support what is typically seen in autism. *Id.* at 177.

Following the entitlement hearing, Petitioner filed a supplemental report from Dr. Chang. In this report, Dr. Chang stated that the video of N.A.C. in Exhibit E does not present as a motor tic. Chang Supplemental Rep. at 1. More pronounced or repetitive movements would be more indicative of a motor tic. *Id.* This video did not change Dr. Chang's opinion of N.A.C.'s condition. *Id.* Even if N.A.C. had motor tics, Dr. Chang stated that he has seen patients with "brief periods of motor tics that then resolve, happening years before the onset of PANS." *Id.* at 1-2.

B. Dr. Donald Gilbert

Respondent filed one expert report and one supplemental report authored by Dr. Donald Gilbert; Ex. A, (hereinafter "Gilbert Rep.") and Ex. C (hereinafter "Gilbert Supplemental Rep."). Dr. Gilbert also provided live testimony at the entitlement hearing.

1. Qualifications

Dr. Gilbert is currently a practicing physician and professor of pediatrics and neurology. Tr. at 205. He graduated *cum laude* in 1987 from Princeton University with an undergraduate degree in philosophy. *Id.* Dr. Gilbert taught high school before attending the University of Michigan for medical school. *Id.* at 205-06. During medical school, he received a Howard Hughes Medical Institute Scholarship to go to the National Institutes of Health to complete an additional year, researching identification of genes involved in the process of HIV infection of brain cells and the cytokines produced by the viruses when exposed to brain cells. *Id.* at 206.

After medical school, Dr. Gilbert completed his residency at Johns Hopkins University in pediatrics and clinical child neurology. Tr. at 207. He holds a board certification in neurology, with a special competence in child neurology. *Id.* After residency, Dr. Gilbert began in his current position as a child neurologist at Cincinnati Children's Hospital Medical Center. *Id.* Hired as an assistant professor, Dr. Gilbert is now a full professor and treats patients with movement disorders. *Id.* at 207-08. More specifically, Dr. Gilbert's practice centers around patients with movement disorders and neuropsychiatric symptoms arising from possible basal ganglia and cerebellar dysfunction. *Id.* at 208. Dr. Gilbert also earned a master's degree in statistics and clinical research design. *Id.* at 207. Additionally, Dr. Gilbert founded the Tourette Syndrome and Movement Disorders Clinic and serves as the director of the Movement Disorder Program. *Id.* at 209.

Outside of his regular practice, Dr. Gilbert has served on several boards and committees, to include the Tourette Syndrome Association Medical Advisory Board, the Tourette Syndrome Association Science Advisory Board, the Child Neurology Society Executive Committee, and the neurology section of the American Academy of Pediatrics. Tr. at 211.

In 2002, Dr. Gilbert was approached to assist in two NIH funded PANDAS research studies. Tr. at 212. He was involved in publications related to those two epidemiologic studies and studies exploring the immune expression profiles of children with Tourette syndrome. *Id.* To date, Dr. Gilbert estimated that he has written about 100 publications. *Id.* at 213.

Dr. Gilbert's most recent publication relating to PANDAS or PANS was an article published in the Journal of Pediatrics in August 2018. Tr. at 213. The same month, he presented grand rounds at his institution on PANDAS and PANS. *Id.* at 214. Dr. Gilbert receives referrals for PANDAS and PANS on a regular basis. *Id.* In total, Dr. Gilbert estimated that he treats about six patients per month where a PANDAS or PANS diagnosis has been considered by the referring physician or the parent. *Id.* at 215.

I recognized Dr. Gilbert as an expert in pediatric neurology and movement disorders. Tr. at 215-16.

2. What is PANS?

Dr. Gilbert testified regarding the history of PANDAS and the emergence of PANS. Tr. at 216. He agreed with Dr. Chang that PANS developed from PANDAS. *Id.* Dr. Gilbert testified, however, that the studies conducted originally by Dr. Swedo, exploring whether strep infections could cause tics or OCD, were flawed in their design and did not definitively answer the question. *Id.* Dr. Gilbert stated that, on the contrary, the studies performed by Dr. James Leckman and Dr. Roger Kurlan better identified and addressed the questions regarding PANDAS at that time: 1) whether an exacerbation of tics or OCD followed identifiable infections, and 2) whether children with PANDAS are different than those with Tourette syndrome or OCD, apart from the waxing and waning of symptoms. *Id.* at 216-17. Dr. Gilbert stated that the studies determined that the onset of exacerbated symptoms did not usually follow a recognizable infection or involvement of the immune system and that there was no clear distinction between children with PANDAS and those with Tourette syndrome. *Id.* at 217-18.

Dr. Gilbert testified that it was the lack of positive results from these studies that led to the formation of PANS, in an effort to capture the children who presented with a "thunderclap onset of severe symptoms" not caused by strep. Tr. at 218. Dr. Gilbert testified, however, that PANS was and still is a working hypothesis regarding this presentation of symptoms. *Id.* at 219. He stated that in his opinion, no autoimmune or inflammatory mechanism had yet been identified as the cause of PANS. *Id.* Furthermore, he testified that the distinguishing factor between PANS patients and OCD or anorexia nervosa patients was the acute onset of the symptoms, but emphasized that no biological way of distinguishing the two had been identified. *Id.*

Dr. Gilbert testified that it was not clear that PANS was a distinct disorder or that PANS could be caused by immune activation. Tr. at 219. Unlike the development of research relating to NMDAR encephalitis, PANS research had not yet identified mechanisms of causation. *Id.* at 220. Dr. Gilbert added that gene identification in Tourette syndrome and autism research had revealed that the identified genes dealt with nerve cell function rather than immune cell function. *Id.* Dr. Gilbert testified that there are no clinical trials showing that the recommended immune-modulating therapy is effective in the treatment of PANS. *Id.* Furthermore, Dr. Gilbert testified that when correctly interpreted, the Parker-Athill study referenced by Dr. Chang illustrates that only one of seven cytokines measured was found to have a marginally significant increase in expression following an onset of symptoms in tic disorder or OCD patients. *Id.* at 224-27.

Dr. Gilbert stated that the assumption of investigators that PANS results from an immune reaction ignores numerous other mechanisms commonly seen in neurologic disorders. Tr. at 220. Dr. Gilbert testified that genetic, mitochondrial, and vascular conditions can also have abrupt onsets, such that an acute onset neurologic condition develops. *Id.* at 232-33.

3. Could Vaccines Have Caused N.A.C.'s Acute Neurologic Disorder?

Dr. Gilbert testified that it is unlikely that N.A.C.'s vaccinations could have triggered a severe cytokine response within 24 hours and caused his acute symptom expression. Tr. at 367. Dr. Gilbert clarified that for Dr. Chang's theory to be possible, the influx of cytokines would have to cross the blood-brain barrier and bypass all other structures of the brain in order to target the basal ganglia within 24 hours. *Id.* at 227-28.

As an initial matter, Dr. Gilbert testified that the theory of the PANS mechanism was atypical when compared to other autoimmune encephalitis conditions. Tr. at 229. He stated that generally autoimmune encephalitis presents with additional symptoms, such as seizures or generalized movement disorders, and not just specific, targeted dysfunction of certain structures within the basal ganglia resulting in only tics and/or OCD. *Id.* at 366. As an example, Dr. Gilbert noted that dysfunction of the basal ganglia, such as with Sydenham's chorea ("SC")[10], results in a presentation of other movement disorders, such as dystonia or chorea. *Id.* at 229-30. It would be unlikely, Dr. Gilbert explained, for basal ganglia dysfunction to be specifically restricted to tics and OCD as a result of an inflammatory response. *Id.* at 366. Dr. Gilbert asserted that this signaled a gap in the understanding of what is actually occurring in a PANS patient. *Id.* at 230.

Dr. Gilbert testified that an abrupt onset of tics or OCD is not atypical. Tr. at 231-32. He stated that neurologic conditions could present acutely without a clear indication of any triggering event. *Id.* at 233-34.

Dr. Gilbert provided a supplemental post-hearing expert report as well. Dr. Gilbert stated that it is difficult to determine if N.A.C. has a motor tic in Ex. E. *Id.* at 1. However, Dr. Gilbert does point out that N.A.C. misuses the pronoun "you," which is a characteristic in children with Autism Spectrum Disorder ("ASD"). *Id.* Dr. Gilbert further stated that the video seems to indicate that "N.A.C. had early signs of ASD that were missed." *Id.* at 1. In addition to the pronoun misuse, N.A.C. "becomes quickly agitated and frustrated, his gait appears somewhat uncoordinated and hypotonic." *Id.* at 1-2. N.A.C. had a history of screaming spells during infancy, and coupled with his agitation in the video, Dr. Gilbert stated that it is possible N.A.C. has sensory hypersensitivity, which is "often seen in children with ASD." *Id.* at 2. Regarding how pre-existing tics would change his opinion, Dr. Gilbert stated that the diagnostic criteria for PANS is "controversial and unsubstantiated," and "it is irrelevant whether tics occurred prior to the vaccination." *Id.* Dr. Gilbert stated that the primary symptoms in a PANS diagnosis are OCD and anorexia, not tics, thus, it is "not highly relevant whether tics occurred prior to vaccination because they are not a core feature of PANS." *Id.* at 2-3. Due to the lack of information of N.A.C.'s neuropsychiatric and developmental status prior to vaccination, Dr. Gilbert does not believe that N.A.C. has PANS but has "an inadequately treated autism spectrum disorder." *Id.* at 3-4.

VI. Applicable Law

A. Petitioner's Overall Burden in Vaccine Program Cases

Under the Vaccine Act, a petitioner may prevail in one of two ways. First, a petitioner may demonstrate that she suffered a "Table" injury—i.e., an injury listed on the Vaccine Injury Table that occurred within the time period provided in the Table. § 11(c)(1)(C)(i). "In such a case, causation is presumed." *Capizzano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1320 (Fed.

[10] Dr. Gilbert discussed Sydenham's chorea briefly at the hearing. First, Dr. Gilbert testified that SC results from a strep infection. The streptococcal bacteria, Dr. Gilbert explained, has numerous proteins on its surface that are similar to those present in the human body, allowing for antibodies to misidentify the foreign agent. SC, therefore, results from the targeted misidentification and destruction of basal ganglia cells following molecular mimicry.

Cir. 2006); *see* § 13(a)(1)(B). Second, where the alleged injury is not listed in the Vaccine Injury Table, a petitioner may demonstrate that he suffered an "off-Table" injury. § 11(c)(1)(C)(ii).

For both Table and non-Table claims, Vaccine Program petitioners bear a "preponderance of the evidence" burden of proof. § 13(1)(a). That is, a petitioner must offer evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence before [she] may find in favor of the party who has the burden to persuade the judge of the fact's existence." *Moberly v. Sec'y of Health & Human Servs.*, 592 F.3d 1315, 1324 (Fed. Cir. 2010); *see also Snowbank Enter. v. United States*, 6 Cl. Ct. 476, 486 (1984) (mere conjecture or speculation is insufficient under a preponderance standard). Proof of medical certainty is not required. *Bunting v. Sec'y of Health & Human Servs.,* 931 F.2d 867, 873 (Fed. Cir. 1991). In particular, a petitioner must demonstrate that the vaccine was "not only [the] but-for cause of the injury but also a substantial factor in bringing about the injury." *Moberly*, 592 F.3d at 1321 (quoting *Shyface v. Sec'y of Health & Human Servs.*, 165 F.3d 1344, 1352 (Fed. Cir. 1999)); *Pafford v. Sec'y of Health & Human Servs.*, 451 F.3d 1352, 1355 (Fed. Cir. 2006). A petitioner may not receive a Vaccine Program award based solely on her assertions; rather, the petition must be supported by either medical records or by the opinion of a competent physician. Section 13(a)(1).

In attempting to establish entitlement to a Vaccine Program award of compensation for a non-Table claim, a petitioner must satisfy all three of the elements established by the Federal Circuit in *Althen v. Sec'y of Health & Human Servs.*, 418 F.3d 1274 (Fed. Cir. 2005). *Althen* requires that petitioner establish by preponderant evidence that the vaccination he received caused his injury "by providing: (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." *Id.* at 1278.

Under *Althen* prong one, petitioners must provide a "reputable medical theory," demonstrating that the vaccine received *can cause* the type of injury alleged. *Pafford*, 451 F.3d at 1355-56 (citations omitted). To satisfy this prong, a petitioner's theory must be based on a "sound and reliable medical or scientific explanation." *Knudsen v. Sec'y of Health & Human Servs.*, 35 F.3d 543, 548 (Fed. Cir. 1994). Proof that a vaccine likely caused an injury or that the proffered medical theory is reasonable, plausible, or possible does not satisfy a petitioner's burden. *Boatmon v. Sec'y of Health & Human Servs.*, 941 F.3d 1351, 1359-60 (Fed. Cir. 2019).

Petitioners may satisfy the first *Althen* prong without resort to medical literature, epidemiological studies, demonstration of a specific mechanism, or a generally accepted medical theory. *Andreu v. Sec'y of Health & Human Servs.*, 569 F.3d 1367, 1378-79 (Fed. Cir. 2009) (citing *Capizzano*, 440 F.3d at 1325-26). However, special masters are "entitled to require some indicia of reliability to support the assertion of the expert witness." *Boatmon*, 941 F.3d at 1360, *quoting Moberly*, 592 F.3d at 1324. Special Masters, despite their expertise, are not empowered by statute to conclusively resolve what are complex scientific and medical questions, and thus scientific evidence offered to establish *Althen* prong one is viewed "not through the lens of the laboratorian, but instead from the vantage point of the Vaccine Act's preponderant evidence standard." *Id.* at 1380. Accordingly, special masters must take care not to increase the burden

placed on petitioners in offering a scientific theory linking vaccine to injury. *Contreras v. Sec'y of Health & Human Servs*., 121 Fed. Cl. 230, 245 (2015).

The second *Althen* prong requires proof of a logical sequence of cause and effect, usually supported by facts derived from a petitioner's medical records. *Althen*, 418 F.3d at 1278; *Andreu*, 569 F.3d at 1375-77; *Capizzano*, 440 F.3d at 1326 ("medical records and medical opinion testimony are favored in vaccine cases, as treating physicians are likely to be in the best position to determine whether a 'logical sequence of cause and effect show[s] that the vaccination was the reason for the injury'") (quoting *Althen*, 418 F.3d at 1280). Medical records are generally viewed as particularly trustworthy evidence, since they are created contemporaneously with the treatment of the patient. *Cucuras v. Sec'y of Health & Human Servs.*, 993 F.2d 1525, 1528 (Fed. Cir. 1993).

However, medical records and/or statements of a treating physician's views do not *per se* bind the special master to adopt the conclusions of such an individual, even if they must be considered and carefully evaluated. Section 13(b)(1) (providing that "[a]ny such diagnosis, conclusion, judgment, test result, report, or summary shall not be binding on the special master or court"); *Snyder v. Sec'y of Health & Human Servs*., 88 Fed. Cl. 706, 746 n.67 (2009) ("there is nothing … that mandates that the testimony of a treating physician is sacrosanct -- that it must be accepted in its entirety and cannot be rebutted"). As with expert testimony offered to establish a theory of causation, the opinions or diagnoses of treating physicians are only as trustworthy as the reasonableness of their suppositions or bases. The views of treating physicians should also be weighed against other, contrary evidence also present in the record -- including conflicting opinions among such individuals. *Hibbard v. Sec'y of Health & Human Servs*., 100 Fed. Cl. 742, 749 (2011) (not arbitrary or capricious for special master to weigh competing treating physicians' conclusions against each other), *aff'd*, 698 F.3d 1355 (Fed. Cir. 2012); *Caves v. Sec'y of Health & Human Servs*., No. 06-522V, 2011 WL 1935813, at *17 (Fed. Cl. Spec. Mstr. Apr. 29, 2011), *mot. for review den'd*, 100 Fed. Cl. 344, 356 (2011), *aff'd without opinion*, 475 Fed. App'x 765 (Fed. Cir. 2012).

The third *Althen* prong requires establishing a "proximate temporal relationship" between the vaccination and the injury alleged. *Althen*, 418 F.3d at 1281. That term has been equated to the phrase "medically-acceptable temporal relationship." *Id.* A petitioner must offer "preponderant proof that the onset of symptoms occurred within a timeframe which, given the medical understanding of the disorder's etiology, it is medically acceptable to infer causation." *de Bazan v. Sec'y of Health & Human Servs*., 539 F.3d 1347, 1352 (Fed. Cir. 2008). The explanation for what is a medically acceptable timeframe must also coincide with the theory of how the relevant vaccine can cause an injury (*Althen* prong one's requirement). *Id.* at 1352; *Shapiro v. Sec'y of Health & Human Servs*., 101 Fed. Cl. 532, 542 (2011), *recons. den'd after remand*, 105 Fed. Cl. 353 (2012), *aff'd mem*., 503 F. App'x 952 (Fed. Cir. 2013); *Koehn v. Sec'y of Health & Human Servs*., No. 11-355V, 2013 WL 3214877 (Fed. Cl. Spec. Mstr. May 30, 2013), *mot. for review den'd* (Fed. Cl. Dec. 3, 2013), *aff'd*, 773 F.3d 1239 (Fed. Cir. 2014).

B. Law Governing Analysis of Fact Evidence

The process for making factual determinations in Vaccine Program cases begins with analyzing the medical records, which are required to be filed with the petition. Section 11(c)(2).

The special master is required to consider "all [] relevant medical and scientific evidence contained in the record," including "any diagnosis, conclusion, medical judgment, or autopsy or coroner's report which is contained in the record regarding the nature, causation, and aggravation of the petitioner's illness, disability, injury, condition, or death," as well as the "results of any diagnostic or evaluative test which are contained in the record and the summaries and conclusions." Section 13(b)(1)(A). The special master is then required to weigh the evidence presented, including contemporaneous medical records and testimony. *See Burns v. Sec'y of Health & Human Servs.*, 3 F.3d 413, 417 (Fed. Cir. 1993) (it is within the special master's discretion to determine whether to afford greater weight to contemporaneous medical records than to other evidence, such as oral testimony surrounding the events in question that was given at a later date, provided that such determination is evidenced by a rational determination).

Medical records created contemporaneously with the events they describe are presumed to be accurate and "complete" such that they present all relevant information on a patient's health problems. *Cucuras*, 993 F.2d at 1528; *Doe/70 v. Sec'y of Health & Human Servs.*, 95 Fed. Cl. 598, 608 (2010) ("[g]iven the inconsistencies between petitioner's testimony and his contemporaneous medical records, the special master's decision to rely on petitioner's medical records was rational and consistent with applicable law"), *aff'd, Rickett v. Sec'y of Health & Human Servs.*, 468 F. App'x 952 (Fed. Cir. 2011) (non-precedential opinion). This presumption is based on the linked propositions that (i) sick people visit medical professionals; (ii) sick people honestly report their health problems to those professionals; and (iii) medical professionals record what they are told or observe when examining their patients in as accurate a manner as possible, so that they are aware of enough relevant facts to make appropriate treatment decisions. *Sanchez v. Sec'y of Health & Human Servs.*, No. 11-685V, 2013 WL 1880825, at *2 (Fed. Cl. Spec. Mstr. Apr. 10, 2013), *mot. for review den'd* (Fed. Cl. Feb. 11, 2019), *appeal docketed*, No. 19-1753 (Fed. Cir. 2019); *Cucuras v. Sec'y of Health & Human Servs.*, 26 Cl. Ct. 537, 543 (1992), *aff'd*, 993 F.2d at 1525 (Fed. Cir. 1993) ("[i]t strains reason to conclude that petitioners would fail to accurately report the onset of their daughter's symptoms.").

Accordingly, if the medical records are clear, consistent, and complete, then they should be afforded substantial weight. *Lowrie v. Sec'y of Health & Human Servs.*, No. 03-1585V, 2005 WL 6117475, at *20 (Fed. Cl. Spec. Mstr. Dec. 12, 2005). Indeed, contemporaneous medical records are generally found to be deserving of greater evidentiary weight than oral testimony -- especially where such testimony conflicts with the record evidence. *Cucuras*, 993 F.2d at 1528; see also *Murphy v. Sec'y of Health & Human Servs.*, 23 Cl. Ct. 726, 733 (1991), *aff'd per curiam*, 968 F.2d 1226 (Fed. Cir. 1992), (citing *United States v. U.S. Gypsum Co.*, 333 U.S. 364, 396 (1947) ("[i]t has generally been held that oral testimony which is in conflict with contemporaneous documents is entitled to little evidentiary weight.")).

However, there are situations in which compelling oral testimony may be more persuasive than written records, such as where records are deemed to be incomplete or inaccurate. *Campbell v. Sec'y of Health & Human Servs.*, 69 Fed. Cl. 775, 779 (2006) ("like any norm based upon common sense and experience, this rule should not be treated as an absolute and must yield where the factual predicates for its application are weak or lacking"); *Lowrie*, 2005 WL 6117475, at *19 ("[w]ritten records which are, themselves, inconsistent, should be accorded less deference than those which are internally consistent") (quoting *Murphy*, 23 Cl. Ct. at 733)). Ultimately, a

determination regarding a witness's credibility is needed when determining the weight that such testimony should be afforded. *Andreu*, 569 F.3d at 1379; *Bradley v. Sec'y of Health & Human Servs.*, 991 F.2d 1570, 1575 (Fed. Cir. 1993).

When witness testimony is offered to overcome the presumption of accuracy afforded to contemporaneous medical records, such testimony must be "consistent, clear, cogent and compelling." *Sanchez*, 2013 WL 1880825, at *3 (citing *Blutstein v. Sec'y of Health & Human Servs.*, No. 90-2808V, 1998 WL 408611, at *5 (Fed. Cl. Spec. Mstr. June 30, 1998)). In determining the accuracy and completeness of medical records, the Court of Federal Claims has listed four possible explanations for inconsistencies between contemporaneously created medical records and later testimony: (1) a person's failure to recount to the medical professional everything that happened during the relevant time period; (2) the medical professional's failure to document everything reported to her or him; (3) a person's faulty recollection of the events when presenting testimony; or (4) a person's purposeful recounting of symptoms that did not exist. *LaLonde v. Sec'y of Health & Human Servs.*, 110 Fed. Cl. 184, 203-04 (2013), *aff'd*, 746 F.3d 1334 (Fed. Cir. 2014). In making a determination regarding whether to afford greater weight to contemporaneous medical records or other evidence, such as testimony at hearing, there must be evidence that this decision was the result of a rational determination. *Burns*, 3 F.3d at 417.

C. Analysis of Expert Testimony

Establishing a sound and reliable medical theory connecting the vaccine to the injury often requires a petitioner to present expert testimony in support of her claim. *Lampe v. Sec'y of Health & Human Servs.*, 219 F.3d 1357, 1361 (Fed. Cir. 2000). Vaccine Program expert testimony is usually evaluated according to the factors for analyzing scientific reliability set forth in *Daubert v. Merrell Dow Pharm., Inc.*, 509 U.S. 579, 594-96 (1993). *See Cedillo v. Sec'y of Health & Human Servs.*, 617 F.3d 1328, 1339 (Fed. Cir. 2010) (*citing Terran v. Sec'y of Health & Human Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999). "The *Daubert* factors for analyzing the reliability of testimony are: (1) whether a theory or technique can be (and has been) tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community." *Terran*, 195 F.3d at 1316 n.2 (citing *Daubert*, 509 U.S. at 592-95).

The *Daubert* factors play a slightly different role in Vaccine Program cases than they do when applied in other federal judicial fora. *Daubert* factors are employed by judges to exclude evidence that is unreliable and potentially confusing to a jury. In Vaccine Program cases, these factors are used in the weighing of the reliability of scientific evidence. *Davis v. Sec'y of Health & Human Servs.*, 94 Fed. Cl. 53, 66-67 (2010) ("uniquely in this Circuit, the *Daubert* factors have been employed also as an acceptable evidentiary-gauging tool with respect to persuasiveness of expert testimony already admitted"). The flexible use of the *Daubert* factors to evaluate persuasiveness and reliability of expert testimony has routinely been upheld. *See*, e.g., *Snyder*, 88 Fed. Cl. at 743. In this matter, (as in numerous other Vaccine Program cases), *Daubert* has not been employed at the threshold to determine what evidence should be admitted, but instead to determine whether expert testimony offered is reliable and/or persuasive.

Respondent frequently offers one or more experts of his own in order to rebut a petitioner's case. Where both sides offer expert testimony, a special master's decision may be "based on the credibility of the experts and the relative persuasiveness of their competing theories." *Broekelschen v. Sec'y of Health & Human Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (citing *Lampe*, 219 F.3d at 1362). However, nothing requires the acceptance of an expert's conclusion "connected to existing data only by the *ipse dixit* of the expert," especially if "there is simply too great an analytical gap between the data and the opinion proffered." *Snyder*, 88 Fed. Cl. at 743 (quoting *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997)). A "special master is entitled to require some indicia of reliability to support the assertion of the expert witness." *Moberly*, 592 F.3d at 1324. Weighing the relative persuasiveness of competing expert testimony, based on a particular expert's credibility, is part of the overall reliability analysis to which special masters must subject expert testimony in Vaccine Program cases. *Id.* at 1325-26 ("[a]ssessments as to the reliability of expert testimony often turn on credibility determinations"); *see also Porter v. Sec'y of Health & Human Servs.*, 663 F.3d 1242, 1250 (Fed. Cir. 2011) ("this court has unambiguously explained that special masters are expected to consider the credibility of expert witnesses in evaluating petitions for compensation under the Vaccine Act").

D. Consideration of Medical Literature

Although this decision discusses some but not all of the medical literature in detail, I reviewed and considered all of the medical records and literature submitted in this matter. *See Moriarty v. Sec'y of Health & Human Servs.*, 844 F.3d 1322, 1328 (Fed. Cir. 2016) ("We generally presume that a special master considered the relevant record evidence even though [s]he does not explicitly reference such evidence in h[er] decision."); *Simanski v. Sec'y of Health & Human Servs.*, 115 Fed. Cl. 407, 436 (2014) ("[A] Special Master is 'not required to discuss every piece of evidence or testimony in her decision.'" (citation omitted)), *aff'd*, 601 F. App'x 982 (Fed. Cir. 2015).

VII. Analysis

Because Petitioner does not allege an injury listed on the Vaccine Injury Table, Petitioner's claim is classified as "off-Table." As noted above, to prevail on an "off-Table" claim, Petitioner must prove by preponderant evidence that N.A.C. suffered an injury and that this injury was caused by the vaccinations at issue. *See Capizzano*, 440 F.3d at 1320.

A. PANS Generally

At hearing, both Dr. Chang and Dr. Gilbert went into extensive detail regarding the history and development of the PANS criteria, as well as the specific diagnostic criteria themselves.

Dr. Chang first described the development of the diagnostic criteria for PANDAS, a syndrome he considers a subset of PANS. He testified that PANDAS arose from a recognition that a subsection of individuals developed a sudden onset of neuropsychiatric symptoms following infection with Group A Streptococcus ("GAS"). Though GAS infection is a known trigger for a

number of disorders,[11] these individuals experienced a definitive, acute onset of neuropsychiatric symptoms following an identified GAS infection.[12]

As both experts indicated, however, the PANDAS criteria failed to encompass individuals who presented with a similar onset of symptoms, yet with no known or identified GAS infection. Ultimately, the criteria for PANS were formulated to incorporate those patients without identifiable GAS infections. For these individuals, literature hypothesizes that while the etiology is currently unknown, various infectious and environmental factors may be causative. Still, the acuity of onset was preserved as a mandatory criterion, as was the requirement that other neurologic disorders cannot better explain the symptoms. The following diagnostic criteria were compiled for PANS:

> I. Abrupt, dramatic onset of obsessive-compulsive disorder or severely restricted food intake
>
> II. Concurrent presence of additional neuropsychiatric symptoms, with similarly severe and acute onset, from at least two of the following seven categories:
>
> 1. Anxiety
> 2. Emotional lability and/or depression
> 3. Irritability, aggression and/or severely oppositional behaviors
> 4. Behavioral (developmental) regression
> 5. Deterioration in school performance
> 6. Sensory or motor abnormalities
> 7. Somatic signs and symptoms, including sleep disturbances, enuresis or urinary frequency
>
> III. Symptoms are not better explained by a known neurologic or medical disorder, such as Sydenham chorea, systemic lupus erythematosus, Tourette disorder or others.

---

[11] Presenting factors such as chorea or manifestations of rheumatic fever were considered exclusionary factors in order to separate PANDAS patients from those with Sydenham's chorea, for example. Swedo et al., *From Research Subgroup to Clinical Syndrome: Modifying the PANDAS Criteria to Describe PANS (Pediatric Acute-onset Neuropsychiatric Syndrome)*, PEDIATRICS & THERAPEUTICS (2012) (hereinafter "Swedo") (filed as Ex. 26).

[12] The following five diagnostic criteria must be met to establish a PANDAS diagnosis:

1. Presence of OCD or a tic disorder
2. Prepubertal symptom onset
3. Acute symptom onset and episodic (relapsing-remitting) course
4. Temporal association between Group A streptococcal infection and symptom onset/exacerbations
5. Associated with neurological abnormalities, (particularly motoric hyperactivity and choreiform movements)

See Swedo.

> Note: The diagnostic work-up of patients suspected of PANS must be comprehensive enough the rule out these and other relevant disorders. The nature of the co-occurring symptoms will dictate the necessary assessments, which may include MRI scan, lumbar puncture, electroencephalogram or other diagnostic tests.

Swedo at 3. *See also* Chang et al., *Clinical Evaluation of Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS): Recommendations from the 2013 PANS Consensus Conference*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 25, No. 1, pp. 3-13 (2015) (filed as Ex. 17).

Both experts confirmed that the etiology and triggering mechanism for PANS are yet unknown. Tr. at 120-21; 218-20. Unlike PANDAS, no specific infectious or environmental factor has been identified. Both experts also confirmed that given the neurologic symptoms involved, it is likely that PANS also involves basal ganglia dysfunction. Dr. Chang asserted that "the predominant – the basic idea is that – is a triggering event, which is either known or unknown, and because of the triggering event there is an inflammatory reaction that for some reason targets the basal ganglia." *Id.* at 116.

Dr. Chang added that PANS developed in individuals with a predisposition, genetic or otherwise, to this type of neuropsychiatric disorder. Though no genetic component has been isolated, Dr. Chang hypothesized that a genetic marker may cause some children to be more susceptible to PANS following triggering events.

Regarding the episodic nature of PANS, further studies hypothesize that chronic static or progressive course may be indicative of different illnesses, as they indicate the involvement of autoimmune, rather than autoinflammatory, processes. Frankovich et al., *Multidisciplinary Clinic Dedicated to Treating Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome: Presenting Characteristics of the First 47 Consecutive Patients*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 25, No. 1, pp. 38-47 (2015) (filed as Ex. 21).

1. PANS versus Tourette syndrome ("TS")

Studies further acknowledge that there may not be a clear distinction between the mechanisms leading to gradual onset of these symptoms, as seen in SC or TS, and the mechanisms resulting in a sudden onset of these symptoms, as observed in PANS or PANDAS patients. As studies regarding PANDAS are more prevalent, the similarities between PANDAS and other neurologic disorders have been repeatedly discussed. The classification of PANDAS as a separate disorder is still widely debated. Researchers and clinicians have considered whether PANDAS is a variant of acute rheumatic fever, and "controversy does exist among some neurologists regarding the validity of PANDAS as a subset of OCD/tics versus its being a forme fruste of RF (SC)." Cox et al., *Antineuronal Antibodies in a Heterogeneous Group of Youth and Young Adults with Tics and Obsessive-Compulsive Disorder*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 25, No. 1, pp. 76-85 (2015) (filed as Ex. 19).

Dr. Chang asserted that N.A.C. did not have TS because the mechanism and presentation of TS is different than that of PANS, and that N.A.C. did not exhibit the presentation usually observed in TS. Tr. at 141. He stated that TS presented gradually, first with an onset of motor tics, followed by vocal tics. *Id.* Comorbidities such as OCD and ADHD arise gradually following tic presentation. *Id.* Dr. Chang continued that the mechanism for TS may differ from that of PANS. *Id.* TS may have an underlying genetic component, as discussed by Dr. Gilbert in his expert report, that makes its development unavoidable. *Id.* at 142. Rather, TS, unlike PANS, does not require a secondary trigger in order for symptoms to present. *Id.* at 143. Dr. Gilbert testified that there is no biological way to distinguish PANS from OCD or anorexia nervosa plus other symptoms. Tr. at 219.

2. Pre-Existing Tics

According to both experts, there are several comorbidities that can coincide with a PANS diagnosis. Dr. Chang testified that it was not uncommon for other neuropsychiatric disorders such as mood disorders, ADHD, or autism to develop in PANS patients. He further added that a prior history of tics would not preclude a diagnosis of PANS, provided that the onset of OCD and two other secondary symptoms was acute.[13] The Swedo article further clarified that the onset of OCD need not be novel. Mild, pre-existing obsessions do not preclude a PANS consideration, either; such symptoms can precede the sudden onset of severe OCD associated with PANS. Swedo at 3. In fact, Dr. Chang indicated that if N.A.C. had pre-existing tics, that would have made him more susceptible to developing PANS. Chang Supplemental Rep. at 1.

Respondent presented testimony from Dr. Gilbert that N.A.C. had vocal and motor tics that pre-dated his October 2012 vaccinations. *See* Tr. at 331-43, 352-60. Ex. F.

> **Q.** Dr. Gilbert, what do you observe in this video?
>
> **A.** So N.A.C. at this point, five months prior to the vaccination, has tics. So there's a number of tics that we see in this video. They're both motor and phonic or vocal tics. One of the tics is a blink. Now all children blink, but in N.A.C.'s case, he draws in extra facial muscles and combines this with a head tipping. So these are classic early tics that we see in patients that either have provisional tic disorder or Tourette syndrome or some other condition that's associated with tics. … Those are like the tics I see in clinic every week.
>
> …
>
> So the blink that N.A.C. does when he blinks and tips his head at the same time, where he tips his head down to the left, so that's not just a blink. That's a blinking tic. That's a classic blinking tic where the brain sends out a patterned message involving a stereotyped group of muscles of the face and neck. That's a tic.

[13] Dr. Chang testified that while tics were often observed in PANS patients, tics were not included as a primary criterion for diagnosis in order to avoid controversy with neurologists treating Tourette syndrome. Tr. at 114.

Tr. at 338, 340, 356. *See* Ex. F.

Petitioner testified that N.A.C. did not have any tics prior to the September 26, 2012 vaccinations. She described that her husband was teaching the children how to whistle between their fingers. Tr. at 381. She stated that N.A.C. never made this noise again after this day. *Id.* at 382.

Dr. Chang also testified about this issue.

> If I never heard that testimony, I would say, boy, that definitely looks and sounds like a tic, someone's making that noise and someone's blinking their eyes, it very well could be. Having heard the explanation and also heard the end part of the video. I'm satisfied that I don't see that necessarily as a tic at all. I mean, it could just be a boy exerting himself making the squealing noise, and when you do that, you tend to close your eyes. If, you know, you're going to make a big, loud noise, it's not abnormal to close your eyes. I didn't notice any -- you know, Dr. Gilbert is definitely more of a tic expert than I am, but I didn't notice anything unusual compared to normal childhood development, if that were the context.

Tr. at 388-89.

Dr. Gilbert's expertise in this area is superior to that of Dr. Chang. I have considered all of the testimony on this point, and while Dr. Gilbert's testimony provides preponderant evidence that N.A.C. experienced tics prior to his September 26, 2012 vaccinations, this issue is not dispositive. Because tics are not a primary criterion for a PANS diagnosis, the existence of tics prior to the allegedly-causal vaccinations does not foreclose a PANS diagnosis.

3. Autism Spectrum Disorder

Respondent presented some evidence that N.A.C. has autism.

a. Medical Records

On August 27, 2013, N.A.C. saw Dr. Loma-Miller at Children's Hospital's neurology office. Ex. 2 at 4. Dr. Loma-Miller noted that Petitioner expressed interest in having N.A.C. evaluated for autism. *Id.* Dr. Loma-Miller's assessment noted N.A.C.'s history of Tourette syndrome and Dr. Loma-Miller "agree[d] with [N.A.C.'s] mom that he may be in the spectrum of autism, but however, it is not clear cut…." *Id.* Dr. Loma-Miller referred N.A.C. to Developmental Pediatrics for an autism evaluation.

On August 11, 2014, N.A.C. was seen at the Children's Hospital pediatric neurology office by Dr. Matthew S. Warren. Ex. 2 at 2. The record notes his routine visits with the office's neurologist, Dr. Loma-Miller, as well as N.A.C.'s history of vocal and motor tics and diagnosis of Tourette syndrome. *Id.* The record indicates a concern that N.A.C. fits into the autism spectrum. *Id.*

b. School Records

Petitioner and N.A.C.'s teacher provided responses on the GARS-3 indicating, in the opinion of the assessor that "it is very likely that [N.A.C.] demonstrates behaviors consistent with an Autism Spectrum Disorder." Ex. 40 at 55. At the end of her report, Ms. Reel indicated that N.A.C. "may be autistic." *Id.* at 55.

c. Dr. Gilbert's Testimony and Supplemental Expert Report

In his supplemental expert report Dr. Gilbert stated that N.A.C. misuses the pronoun "you," which is a characteristic in children with Autism Spectrum Disorder. Gilbert Supplemental Rep at 1. Dr. Gilbert further stated that the video seems to indicate that "N.A.C. had early signs of ASD that were missed." *Id.* In addition to the pronoun misuse, N.A.C. "becomes quickly agitated and frustrated, his gait appears somewhat uncoordinated and hypotonic." *Id.* at 1-2. N.A.C. had a history of screaming spells during infancy, and coupled with his agitation in the video, Dr. Gilbert stated that it is possible N.A.C. has sensory hypersensitivity, which is "often seen in children with ASD." *Id.* at 2.

This supplemental expert report is in line with Dr. Gilbert's testimony at hearing, where he indicated that N.A.C.'s abnormal speech and other behavior was consistent with autism spectrum disorder. *See* Tr. at 240. *See also id.* at 238 where Dr. Gilbert testified that "tics happen a lot in kids with autism."

d. The Significance of Autism with Respect to a PANS Diagnosis

Ultimately, while it may be more likely than not that N.A.C. has autism, it is not necessary for me to reach that determination. Respondent's expert stated that children with ASD are more likely to develop tics and OCD. Dr. Gilbert testified:

> And what has been shown in the past year is that a number of genes are in common between autism and Tourette syndrome, so that they may not really be so distinct as we have thought they were clinically. That said, as I have mentioned, we see a lot of kids with autism that have tics, and a lot of kids that have tics that show some of the symptoms of autism. So I think those genetic findings kind of confirm a common clinical observation.

Tr. at 362-63; *see also* Gilbert Supplemental Rep. at 1 where Dr. Gilbert states that "children with ASD commonly have tics".

While an autism diagnosis could explain the likelihood that a child will later develop tics and/or OCD, it does not, in and of itself, rule out a PANS diagnosis.

B. N.A.C. Meets the Diagnostic Criteria for PANS

During the hearing, both experts testified at length regarding the diagnostic criteria for PANS. Both Dr. Chang and Dr. Gilbert agreed that PANS was the acute onset of severe OCD or food restriction, accompanied in time by two of the seven secondary criteria. The experts added

that a PANS diagnosis can only arise when another neuropsychiatric disorder cannot better explain the individual's symptoms. Dr. Chang and Dr. Gilbert agreed that N.A.C. experienced a sudden onset of neuropsychiatric symptoms that could not easily be defined by current presentation descriptions of known psychiatric disorders. Dr. Gilbert did note, however, that while not common, tics and/or TS can manifest in a similar acute manner.

Dr. Chang testified that N.A.C. presented with sudden onset of symptoms on October 9, 2019. When reviewing N.A.C.'s PANS presentation, he confirmed that in his opinion, N.A.C. met each of the criteria and subcategories required for a PANS diagnosis. First, Dr. Chang confirmed that N.A.C.'s symptom presentation met the definition of acute onset. Dr. Chang identified N.A.C.'s repetitive behaviors as examples of OCD. Dr. Chang added that N.A.C. also exhibited patterns of food restriction, though less assuredly since weight loss was not noted in the records. N.A.C.'s OCD patterns of behavior, however, satisfied the first PANS criterion. Dr. Chang then testified that N.A.C. exhibited symptoms in each of the seven subcategories of the secondary PANS criteria. Dr. Gilbert agreed that N.A.C.'s presentation satisfied the requirement of concurrent presence of additional neuropsychiatric symptoms, although he testified that N.A.C. met four, as opposed to seven of the secondary criteria. Tr. at 317. Finally, when discussing whether N.A.C. met the third PANS criterion, Dr. Chang explained that he did not believe any other illness better described N.A.C.'s condition.

Dr. Gilbert stated that in his view "the evidence does not support that N.A.C. has a primary tic disorder." Gilbert Supplemental Rep. at 2. He also wrote in his supplemental expert report, "I do not believe that N.A.C. has PANS." *Id.* However, this statement is contrary to a portion of Dr. Gilbert's testimony at hearing.

> **Q.** So based off of everything you just said, do you think that N.A.C. in this case has PANS?
>
> **A.** Yes. He has an acute neuropsychiatric syndrome. What I don't think is that we have any reason to think that his syndrome is immune-mediated or was caused by a vaccine.

Tr. at 221. While this testimony took place before Dr. Gilbert saw the videos of N.A.C. exhibiting what he described as pre-existing tics, his initial statement that N.A.C. has PANS was not explained or clarified.

Based on the available record and the testimony of both witnesses, I find Petitioner has provided preponderant evidence that N.A.C. had a sudden onset of neuropsychiatric symptoms and that such symptoms generally meet the current diagnostic criteria for PANS. First, and in accordance with Dr. Chang's testimony, I find that N.A.C.'s symptoms sufficiently satisfy the three diagnostic criteria for PANS. N.A.C. presented to the emergency room on October 9, 2012 with an acute onset of neuropsychiatric symptoms. Specifically, Petitioner reported to the provider that N.A.C. had recently developed repetitive behavior, accompanied by motor tics, emotional lability, and anxiety. At the hearing, Petitioner testified that these behaviors began approximately 30 hours after vaccination. Though there is evidence that N.A.C. already had tics prior to his September 26, 2012 vaccinations, Petitioner successfully established that the remainder of the

symptoms reported at that appointment developed acutely. Notably, the record indicates that N.A.C.'s symptoms on that date included OCD-type behavior and at least two of the secondary symptoms, emotional lability and anxiety. *See* Ex. 5 at 1-5. Finally, since PANS involves the acute onset of this specific grouping of symptoms, I find, in accordance with Dr. Chang's testimony, that the PANS diagnostic criteria best describe N.A.C.'s presentation.

C. Petitioner has not Carried her Burden of Proof

1. *Althen* Prong 1: There is not Preponderant Evidence that Vaccines Can Cause PANS

As stated repeatedly in the literature, the etiology and mechanism for PANS is unknown. Studies suggest that, as is the case for PANDAS, similar infections may serve as possible PANS triggers. Frankovich at 44. In PANDAS, the mechanism for causation has been identified and is comparable to that of SC. Cross-reaction with group A beta-hemolytic streptococcus infection leads to production of autoantibodies against lysoganglioside and increased activation of calmodulin-dependent protein kinase II (CaMKII). Targeted receptors on the neuronal cells of the basal ganglia may lead to altered dopamine production and basal ganglia dysfunction resulting in abnormal movement. In fact, autoimmunity is a possible mechanism in several disorders with similar presentations, as antineuronal antibodies have been implicated in tic and OCD development associated with strep infections, and significantly higher ANA levels are observed in SC, OCD, and Tourette syndrome patients. *See* Cox at 1; Cunningham and Cox, *Autoimmunity against dopamine receptors in neuropsychiatric and movement disorders: a review of Sydenham chorea and beyond*, ACTA PHYSIOL 2016, 216, pp. 90–100 (filed as Ex. 20); Kirvan et al., *Antibody-mediated neuronal cell signaling in behavior and movement disorders*, JOURNAL OF NEUROIMMUNOLOGY 179 (2006), pp. 173–179 (filed as Ex. 24). Furthermore, such a mechanism for causation explains the development of specific symptoms rather than generalized evidence of basal ganglia dysfunction.

Studies exploring the triggering event and mechanism for PANS are much less common, however. Though inflammation continues to be a hypothesis for PANS causation, the mechanism for inflammation is yet unknown. Frankovich et al., *Five Youth with Pediatric Acute-Onset Neuropsychiatric Syndrome of Differing Etiologies*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 25, No. 1, pp. 31-37 (2015) (filed as Ex. 22). For example, several studies have indicated that PANS may also develop following a mycoplasma infection, suggesting that similar cross-reaction mechanisms may be involved with other infectious agents apart from strep infection. Kim et al., *Obsessive-Compulsive Disorder Related to Mycoplasma-Associated Autoimmune Encephalopathy with Basal Ganglia Involvement*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 26, No. 4, pp. 400-02 (2016) (filed as Ex. 23).

At hearing, Dr. Chang proffered a theory of causation by which PANS may develop following vaccination. Dr. Chang posited that the influx of cytokines following vaccination led to a severe inflammatory response by which the blood brain barrier was penetrated and the basal ganglia was targeted. Dr. Chang testified:

> I can't be sure at all about the exact mechanism behind it. … I would say that the immune stimulation somehow led to an inflammatory reaction that crossed the

> blood-brain barrier and affected probably the basal ganglia, among other areas, of the child's brain and led to this acute inflammatory neuropsychiatric condition.

Tr. at 196-97.

Dr. Chang's theory that PANS occurs following vaccinations involves several steps. First, vaccinations result in the release of cytokines. Second, cytokines increase the permeability of and then cross the blood brain barrier. Third, in genetically-susceptible individuals, cytokines cause targeted inflammation of the basal ganglia. Fourth, this targeted inflammation causes PANS.

a. Does Vaccination Promote the Production of Cytokines?

It is established in the Vaccine Program that vaccination does promote the production of cytokines, although I note that Petitioner did not file literature on this point. Dr. Chang eludes to cytokine production in his testimony when he says, "the trigger [vaccination] triggers an immune reaction that then leads to the whole inflammatory cascade, including cytokine – inflammatory cytokine production…" Tr. at 121. While some cytokine production is a normal vaccine reaction, there is no indication in the record regarding the level of production necessary to lead to an inflammatory cascade.

I note that special masters have found general cytokine-based theories of causation are not persuasive. *Zumwalt on behalf of L.Z. v. Sec'y of Health & Human Servs*., No. 16-994V, 2019 WL 1953739, at *18 (Fed. Cl. Spec. Mstr. Mar. 21, 2019) (noting that "[t]he fact that vaccines are known to stimulate cytokine production . . . does not amount to a reliable causation theory that such stimulation is necessarily disease-causing"); *Inamdar v. Sec'y of Health & Human Servs*., No. 15-1173V, 2019 WL 1160341, at *17 (Fed. Cl. Spec. Mstr. Feb. 8, 2019) (noting that the proposition that vaccines can cause diseases by "induc[ing] the production of proinflammatory cytokines . . . has several deficiencies"); *McCabe v. Sec'y of Health & Human Servs*., No. 13-570V, 2018 WL 3029175, at *47-55 (Fed. Cl. Spec. Mstr. May 17, 2018); *McGuire v. Sec'y of Health & Human Servs*., No. 10-609V, 2015 WL 6150598 at *12-18 (Fed. Cl. Spec. Mstr. Sep. 18, 2015) (noting that the petitioner had failed to introduce "persuasive evidence to rebut the IOM's conclusion that no evidence supports a conclusion that cytokines cause a disease").

As Chief Special Master Corcoran noted in *Dean v. Sec'y of Health & Human Servs*., "The most immediately apparent weakness in this case's causation theory is the heavy lifting it assigns to the post-vaccination cytokine production process as the cause of almost all of the pathologic effects of the vaccines at issue." *Dean v. Sec'y of Health & Human Servs*., No. 13-808V, 2017 WL 2926605, at *16 (Fed. Cl. Spec. Mstr. June 9, 2017). The same is true in Petitioner's case. There has been no testimony helpful to Petitioner's theory regarding the level of cytokine production after vaccination. In fact, when asked whether he knew "the level of cytokine creation that happens after vaccination," Dr. Chang responded, "No, I'm not familiar with the exact level…" Tr. at 160. Accordingly, while I believe it has been established that vaccination induces cytokine production, Petitioner has not presented evidence through her expert or through literature as to the level of that production, or what level is required to be pathologic.

b. Do Cytokines Increase the Permeability of the Blood-Brain Barrier?

While Petitioner did address the question as to whether vaccination can lead to permeability of the blood-brain barrier, the analysis was cursory.

> **Q.** Is the proinflammatory cytokine tumor necrosis factor alpha expressed after vaccination?
>
> **A.** Yes, it is.
>
> **Q.** Can the same proinflammatory cytokines cause the blood-brain barrier to become more permeable?
>
> **A.** They can, yes.

Tr. at 123-24. There was no further discussion on this point, and no literature was filed in support of the proposition that cytokines result in increased permeability of the blood-brain barrier.[14]

In order for cytokine expression to so severely alter the function of the basal ganglia, pro-inflammatory cytokines present at the site of vaccination must then enter the bloodstream and cross the blood-brain barrier at a particularly weak juncture. As the cells supporting the blood-brain barrier form "very tight junctions," Dr. Gilbert testified that these junctions would first need to be loosened before cytokines can cross and "produce inflammation" in basal ganglia structures. Tr. at 228. Dr. Chang stated that he was not able to provide an explanation regarding how this process occurs. (Stating "somehow they [the antibodies] would get past the blood-brain barrier…" and "I don't think the answers [how cytokines cross the blood-brain barrier] are that clear.") *Id.* at 120, 160. Dr. Gilbert, however, added that he found it unlikely such processes could occur in the span of 24 hours. *Id.* at 228.

The ability of cytokines to cross the blood-brain barrier has been discussed in numerous cases in this Program. Special Master Moran in *McGuire* considered the ability for TNF-α, in particular, to cross the blood-brain barrier. *McGuire v. Sec'y of Health & Human Servs.*, No. 10-609V, 2015 WL 6150598 (Fed. Cl. Spec. Mstr. Sept. 18, 2015). In a similar fashion to Dr. Chang, Petitioner's expert in *McGuire* failed to provide an explanation as to how TNF crosses the blood-brain barrier or the method by which it may create permeability of the blood-brain barrier. Due to the lack of a reliable theory for how cytokines may cross the blood-brain barrier following HPV vaccination, Special Master Moran discounted that aspect of Petitioner's theory. *Id.* at *14. In the present case, I find that Petitioner similarly has failed to provide a sound and reliable explanation by which vaccination-induced cytokine expression can lead to cytokines traversing the blood-brain barrier.

[14] In *Dean*, 2017 WL 2926605, Chief Special Master Corcoran discussed a study upon which Petitioners relied to show how cytokines could increase the permeability of the blood-brain barrier. He ultimately found that even with literature filed addressing the issue, "it [was] not enough by itself to establish preponderant evidence that vaccination would more likely than not allow permeation of the blood-brain barrier simply due to cytokine upregulation expected to be caused by the vaccine." *Dean*, 2017 WL 2926605, at *17. No such literature was filed in this case.

c. Does an Upregulation in Cytokines Cause PANS?

Petitioner failed to present preponderant evidence that rapid cytokine cascade and generalized inflammatory response to vaccinations is a likely mechanism by which targeted basal ganglia dysfunction can result. While a "link between inflammation and psychiatric disorders" has been noted (*See* Chang et al., *Special Issue on Pediatric Acute-Onset Neuropsychiatric Syndrome*, JOURNAL OF CHILD AND ADOLESCENT PSYCHOPHARMACOLOGY, Vol. 25, No. 1, pp. 1-2 (2015) (filed as Ex. 18)), there is not preponderant evidence that generalized inflammation can result in the targeted dysfunction observed in disorders of the basal ganglia. Specifically, no theory was presented as to how or why generalized cytokine expression would target only certain basal ganglia structures. Dr. Chang generally stated that the basal ganglia may have been accessible due to its proximity to vascular structures of the brain adding that "we don't know exactly why it would attack the basal ganglia." Tr. at 120.

In fact, Dr. Gilbert described this part of Dr. Chang's theory as "unlikely." Tr. at 366. Dr. Gilbert stated:

> So in the rare cases that we see in centers like ours where there is an encephalitis that is triggered by something and causes inflammation and psychiatric symptoms, those symptoms are not restricted to the symptoms on the PANS list. There are always additional symptoms like seizures, like loss of motor skills to a much more extreme degree, like movement disorders besides tics. He didn't have any of those. So, therefore, I think it's unlikely.

Id.

In attempting to link cytokine production with PANS, Petitioner filed a study measuring cytokine expression in youth with tic disorders which found elevated levels of TNF-α during symptom exacerbation compared to levels during remission. The study was conducted on a total of 21 individuals, and the results for TNF were the only statistically significant value.[15] Indeed, the authors of the study concluded that "despite [the] findings, some disagreement still exists… [S]ome groups… have noted no correlations between TNF and tic disorder." Parker Athill at 5. Dr. Gilbert discussed this study during the hearing, and noted that:

> [T]he problem when you do a big study and you do a lot of comparisons is you have some findings that are statistically different by chance, particularly if you have a small sample like you have in this paper where you don't have that many kids in either group. So we have one P value out of seven that's barely significant in two small groups of papers, and that is sort of the level of evidence that we have about cytokines being part of this process.

Tr. at 226-27.

[15] P value for TNF was 0.05, the threshold value for significance measurements. Dr. Gilbert testified that "out of all two, three, four, five, six, seven cytokines there, there's only one that reached that threshold. How much below that threshold is it? It's right at the threshold. It's at the 5 percent threshold." Tr. at 226.

Regardless of the findings, the results of this study may not be extrapolated so far as to suggest that cytokine expression is involved in the inciting processes of PANS. The study found that TNF was elevated during tic exacerbation. It is not clear from the study whether TNF caused tic exacerbation or whether it was a by-product. This study also does not suggest that vaccinations incite rapid cytokine cascades that result in targeted inflammation of the basal ganglia.

There is scant evidence to suggest that vaccinations may serve as triggering events for PANS or that cytokine expression is even a significant factor in movement disorders or similar neurologic disorders. A survey of PANS patients provided self-reported data of PANS flare-up following flu vaccination. Calaprice at 1. The article aimed to survey purported PANS patients to determine what may have caused their disease. One main flaw with the paper (the authors did not include an epidemiologist or an immunologist), is that the authors trust the participants who filled out the survey did in fact have PANS. Tr. at 253. Dr. Gilbert noted that some of the participants did not have the acute component of PANS, meaning their symptoms were reported as chronic. *Id.* at 254. He summarizes the issues with this study by stating, "There was no attempt made to verify independently the cause (patient-reported antecedent events) or the effect (meeting the criteria for PANS), the temporal interval, the "dose," or the presence or chronicity of other behavioral diagnoses."[16]

Additionally, Petitioner filed the Leslie article, which found that the onset of some neuropsychiatric disorders may be temporally related to prior vaccinations. Leslie at 1. Dr. Gilbert testified as to the "major flaws" associated with this study. *See* Tr. at 242. The authors of the study (an economist, an attorney/philanthropist, and two psychiatrists, with the notable lack of participation from an immunologist and an epidemiologist) looked at the associations between vaccines and medical events. As a control, they chose two events that one would assume could not be related to vaccines (broken bones and open wounds). *Id.* at 245. They also selected conditions related to PANS and PANDAS such as anorexia nervosa, tics, and OCD. Dr. Gilbert testified that the results indicated that you were 7% more likely to have suffered a broken bone if you had received a vaccination in the past 12 months. *Id.* at 246. Further, the results from the study also indicate that you are 11% less likely to suffer from depression if you had received a vaccine in the past 12 months. *Id.* at 247. According to Dr. Gilbert, these findings "make me think, hmmm, maybe there's a problem with the way this study was designed." *Id.* at 246. In summary, Dr. Gilbert testified convincingly that the results of this study were not reliable and constituted "statistical noise." *Id.* at 247.

Petitioner also discussed an article that Dr. Gilbert wrote with four other authors (*See* Martino et al., *Immunopathogenic Mechanisms in Tourette Syndrome: A Critical Review*, MOV DISORD. 2009, pp. 1267–79, (filed as Ex. 44)). In that article, the authors hypothesize that "symptoms observed in TS patients, such as tics, OC symptoms, and depressive/anxiety symptoms, might also be directly or indirectly precipitated by cytokines." *Id.* at 9. The conclusion of the one paragraph devoted to a discussion of cytokines in this ten-page article states, "However,

[16] Gilbert et al., *A Pediatric Neurology Perspective on Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infection and Pediatric Acute-Onset Neuropsychiatric Syndrome*, THE JOURNAL OF PEDIATRICS, May 21, 2018 (filed as Ex. C, Tab 4).

currently clear evidence of cytokine-induced neural dysfunction in TS is lacking and should be addressed in future studies." *Id.* This article is consistent with Dr. Gilbert's testimony at hearing that Dr. Chang's proposed causative mechanism is no more than a hypothesis.[17] Tr. at 219.

While the exact role of cytokines in this process is investigated, literature has yet to support cytokine expression as a sound and reliable theory of causation in the development of PANS. As Dr. Gilbert testified at hearing, "there's no evidence of cytokine expression involvement in PANS that's credible." Tr. at 375-76. Petitioner is not required to produce medical literature to establish vaccine causation. When literature is submitted, the special master can consider that literature as part of the *Althen* prong 1 analysis. *Andreu*, 569 F.3d at 1379. Along the same lines, there is not any consensus regarding the role of inflammation in causing tics or OCD.[18] It is, therefore, not clear what, if any, factors can serve as triggering events for PANS and how such triggering events cause PANS. Proof that the proffered medical theory is plausible or possible does not satisfy a petitioner's burden. *See Boatmon*, 941 F.3d at 1359-60.

I do not find it probable that PANS can be caused by a cytokine cascade and, as such, find that Petitioner failed to meet her burden in presenting preponderant evidence linking N.A.C.'s vaccinations to PANS under *Althen* prong 1.

d. Molecular Mimicry

Although only addressed in passing, Petitioner's expert did discuss the concept of molecular mimicry as a potential causation mechanism for PANS. During the initial part of his direct examination, Dr. Chang discussed two hypothetical mechanisms, that he described as immunologic and inflammatory. In the immunologic mechanism (molecular mimicry), the antigens "look a little bit enough like the host brain tissue that the host would make antibodies against that, thinking that that might be a defense mechanism." Tr. at 119. During his testimony, Dr. Chang clarified that his causative theory in this case was the inflammatory theory. Dr. Chang testified as follows:

> **Q.** So you wrote in your report that PANS is thought to be inflammatory and/or immunologic. And in this case in particular, it sounds like you're saying you think this is more of the inflammatory –

[17] Several times during the hearing, Dr. Gilbert referenced "high quality scientific literature" and "class I evidence" and getting to "99 percent" regarding a theory. Tr. at 219, 221, 227. I recognize that this level of evidence is not required in the Vaccine Program, and that instead, Petitioner is required to present a sound and reliable theory that establishes each *Althen* prong by preponderant evidence. I have applied that standard in this case.

[18] *See* Donald L. Gilbert, MD, MS, *Inflammation in Tic Disorders and Obsessive-Compulsive Disorder: Are PANS and PANDAS a Path Forward?*, JOURNAL OF CHILD NEUROLOGY, 2019 (filed as Ex. C, Tab 3) stating, "At this time, among highly experienced and respected clinicians and researchers spanning relevant disciplines, there is substantial controversy regarding a role for inflammation in producing tics and obsessive-compulsive disorder." Dr. Gilbert's testimony at hearing was similar: "to date we don't have evidence that PANS is an inflammatory disorder. That's an ongoing area of investigation. Some PANS cases may turn out to be inflammatory over the next 20 years, some may not. It may not be inflammatory at all." Tr. at 376.

A. Inflammatory, exactly. Right.

Q. So why do you say that in this specific case?

A. I would say that more because of the acuity of the symptoms. The cytokine reaction is so quick. The inflammatory reactions are so quick. … But I would say because of that, it makes more sense to me that this would be something that would be more cytokine/inflammatory cascade-related than something that would be more antibody cross-reacting, which often can take a little bit longer. I understand – my understanding is limited in that area, but I understand some other disorders can take longer to manifest in which there is molecular mimicry or antibody [sic] that actually cross react.

Q. So when you talk about the production of antineuronal antibodies … is that for the immune-mediated response?

A. That's more for the immune – what we think about is the, right antibody mediator response.

Tr. at 191-92.[19] Based on Dr. Chang's own testimony, I do not find molecular mimicry to be a viable causation theory in this case. The onset of symptoms so quickly after vaccination is not consistent with the adaptive immune response inherent in the theory of molecular mimicry.[20]

2. *Althen* Prong 2: There is not Preponderant Evidence that N.A.C.'s Vaccinations Did Cause PANS

The second *Althen* prong provides that petitioners must demonstrate by a preponderance of the evidence that there is "a logical sequence of cause and effect" between the vaccination and the illness. *Althen*, 418 F.3d at 1278. I note at the outset that my findings with respect to the first *Althen* prong make it impossible for me to conclude that Petitioner successfully established that N.A.C.'s vaccines "did cause" his PANS. However, even assuming I had determined that Petitioner successfully established a sound and reliable medical theory, she still has not

[19] Dr. Chang testified about his support for an inflammatory theory of causation several times during the hearing. *See also* Tr. at 159-60, 203.

[20] *See Mosley v. Sec'y of Health & Human Servs.*, No. 08–724V, 2015 WL 2354316 (Fed. Cl. Spec. Mstr. Apr. 27, 2015) (finding onset of TM one day after tetanus vaccination was too soon to support the immune activation required for vaccine causation); *Crosby v. Sec'y of Health & Human Servs.*, No. 08–799V, 2012 WL 13036266 (Fed. Cl. Spec. Mstr. June 20, 2012) (finding a 24-hour window between vaccination and symptom onset was not medically appropriate in the context of a molecular mimicry theory); *Flores v. Sec'y of Health & Human Servs.*, No. 10–489V, 2013 WL 5587390 (Fed. Cl. Spec. Mstr. Sept. 12, 2013) (finding the cause of a stroke one day after vaccination could not have been immune-mediated inflammation), *aff'd*, 115 Fed. Cl. 157 (2014).

preponderantly demonstrated a logical sequence of cause and effect between N.A.C.'s vaccinations and his illness.

a. Treating Physicians

In weighing evidence, special masters are expected to consider the views of treating doctors. *Cappizano v. Sec'y of Health & Human Servs.*, 440 F.3d 1317, 1326 (Fed. Cir. 2006). The views of treating doctors about the appropriate diagnosis are often persuasive because the doctors have direct experience with the patient whom they are diagnosing. *See McCulloch v. Sec'y of Health & Human Servs.*, No. 09-293V, 2015 WL 3640610, at *20 (Fed. Cl. Spec. Mstr. May 22, 2015).

In this case, no treating physician has diagnosed N.A.C. with PANS. Setting the diagnosis aside and looking to the underlying symptoms, no treating physician has attributed any of N.A.C.'s tics or OCD to his vaccinations. In fact, on October 15, 2012, Dr. Loma-Miller (a neurologist) assessed N.A.C. and specifically stated "I explained to the mother that I do not think that these abnormal movements are related to the vaccines. There was no specific data in the medical literature to support such concerns." Ex. 2 at 11. No other treating physician commented on N.A.C.'s PANS (or any symptoms associated with PANS) as developing from the vaccines he received.[21]

b. There is no Medical Record Evidence that N.A.C. Experienced Immune Activation

Dr. Chang's prong 1 theory of causation is that cytokines produced after vaccination crossed N.A.C.'s blood-brain barrier, targeted the basal ganglia, and resulted in PANS. However, Dr. Chang admitted that there was no evidence that any of these steps occurred in N.A.C.'s case. Dr. Chang testified, "That's correct. There's no way of knowing [the level of cytokines created in N.A.C.'s case post-vaccination] for sure unless he had his blood drawn for those factors at that time." Tr. at 160. When asked "Is there any evidence of permeability of the blood-brain barrier having that characteristic in N.A.C.'s case?" Dr. Chang responded, "Not that I'm aware of." *Id.* at 161. Finally, when asked "How would we know if there was inflammation in N.A.C.'s basal ganglia?" Dr. Chang responded that brain imaging would have needed to have been done very quickly. He acknowledged that it was not done in this case. *Id.* at 162.

As Dr. Gilbert noted in his expert report, "in N.C.'s case, there are no medical diagnostic tests that support that his immune system was activated in any unusual, disease-causing way. There was no immune testing done at all." Gilbert Rep. at 13. While these test results may not be

[21] Petitioner testified at hearing that the ER doctor told her "there's a possibility" N.A.C.'s vaccinations caused his onset of symptoms. Tr. at 26. She further testified that her family doctor also indicated N.A.C.'s vaccinations could have caused his tics and OCD: "And I asked Dr. John, I said, Dr. John, could vaccines cause this? And he said, yes, there's a good possibility." Tr. at 31. I decline to credit this testimony over the contemporaneous medical records, which do not reference such comments. *See* Ex. 5 at 1-18; Ex. 8 at 3-4.

necessary for Petitioner to meet her burden under *Althen* prong 2, the lack of such evidence does not advance Petitioner's case.

Further, there is no indication that N.A.C. showed any reaction to the vaccinations he received. The medical records do not suggest that he developed a post-vaccination fever or malaise. In other words, there is no indication in N.A.C. of a release of cytokines above that which would normally be expected to occur. The only support that Petitioner provides in asserting that there is a logical sequence of cause and effect between the vaccinations and the injury is the injury itself coupled with its temporal proximity to vaccination. This showing is insufficient. For the reasons discussed above, there is not preponderant evidence of a logical sequence of cause and effect between the vaccinations that N.A.C. received and his development of PANS. Petitioner has therefore failed to sustain her burden under *Althen* prong 2.

3. *Althen* Prong 3: Petitioner has not Demonstrated that N.A.C. Developed PANS in a Medically-Appropriate Onset Interval after Vaccination

The timing prong contains two parts. First, a petitioner must establish the "timeframe for which it is medically acceptable to infer causation" and second, he must demonstrate that the onset of the disease occurred in this period. *Shapiro v. Sec'y of Health & Human Servs.,* 101 Fed. Cl. 532, 542-43 (2011), *recons. denied after remand on other grounds*, 105 Fed. Cl. 353 (2012), *aff'd without op.,* 503 F. App'x 952 (Fed. Cir. 2013). I find that Petitioner has not established the timeframe for which it is medically acceptable to infer causation, and because of this has not established that N.A.C. developed PANS in such a medically-accepted time period.

a. N.A.C. Developed PANS the Day after his Vaccinations

N.A.C. received his vaccinations on September 26, 2012. Petitioner informed Dr. Loma-Miller that N.A.C. "started having episodes of abnormal movements consisting of neck flexion, shoulder shrugging and throat clearing episodes" on September 27, 2012. Ex. 2 at 10. Consistent with this entry in the medical records, Petitioner testified at hearing that N.A.C. experienced a reaction the next day after his vaccinations, approximately 30 hours later. Tr. at 15.

b. Petitioner has not Established the Timeframe for which it is Medically Acceptable to Infer Causation

While the record establishes that N.A.C. developed his first symptoms of PANS approximately one day after his vaccinations, neither expert spent much time discussing the medically-appropriate interval between vaccination and onset of PANS. Dr. Chang provided limited testimony on this issue.

> **Q.** So what about the triggering event. Is there anything in your research or in the literature that talks about the triggering event and then onset –
>
> **A.** That it has to be within a certain amount of time of the actual – not per se. That's something that we've talked about. For example, we use strep as the best example of that. We always say, well, how soon after a strep infection do you need

> to have this happen? And unfortunately, there's been no consensus about that because it seems like there's a variety of presentations that can happen the day after you get, you know, a sore throat. It can happen the week after you get the sore throat and a fever.
>
> I would say that usually anything more than a few weeks after it would be very unlikely to be that case. So in my personal opinion, I would say usually it's one to two weeks. However, that's, again, not born out by any research or even by consensus because people have different opinions on that.

Tr. at 188. It is unclear why Dr. Chang discussed one to two weeks when onset in this case took place approximately one day after vaccination. It is possible Dr. Chang was referring to onset of symptoms in a case that developed during molecular mimicry.

Dr. Chang did provide additional testimony regarding prong 3 when questioned by Petitioner's counsel on redirect examination.

> **Q.** How rapid is cytokine expression following vaccination?
>
> **A.** Oh. Again, I'm not a vaccination expert. But my understanding is that following any kind of this type of provocation with antigen, whether live or dead, you get very rapid cytokine response. …
>
> **Q.** Hours? Days?
>
> **A.** Yeah. I would say within hours.
>
> **Q.** Does that – so given the rapidity of onset, if you assume that vaccination was the triggering event and symptoms manifested within a day or so post-vaccination, does the cytokine expression theory explain the rapid acute onset then?
>
> **A.** Well, it indicates that, yes, you would have the rapid inflammatory cascade. And so, yes, it does in my mind explain that. One possibility of why it's so rapid.

Tr. at 203. While this testimony does suggest that Dr. Chang believes 24 hours is an appropriate temporal onset interval based on the causation theory he presented, this testimony merely states his belief. A special master is not required to accept an expert's *ipse dixit*. *Snyder*, 88 Fed. Cl. at 743. Dr. Chang does not explain how a rapid cytokine response can cause onset of PANS in one day. Although not required, he also does not cite to any literature in support of this proposition. In fact, it is difficult to square this testimony with Dr. Chang's earlier statement that there was "no consensus" about an appropriate onset interval. *Id.* at 188. Thus, Petitioner has not established that *Althen* prong 3 has been met in this case based on Dr. Chang's say-so. She instead needed to establish that this opinion constituted a sufficiently reliable medical or scientific explanation. The evidence presented was insufficient in this regard.

Further, Dr. Gilbert testified he believed onset in approximately one day was "unlikely." Tr. at 366. He specifically testified that "the proposed mechanism of a vaccine causing a change in the brain that quickly that's restricted to tics and OCD symptoms, seems to me extremely unlikely based on my experience with other things that have a biological marker like NMDA receptor encephalitis." *Id.*

Petitioner does not meet her burden by simply showing a proximate temporal association between the vaccination and the injury. *Grant*, 956 F.2d at 1148 (quoting *Hasler v. United States*, 718 F.2d 202, 205 (6th Cir. 1983), cert. denied, 469 U.S. 817 (1984) (stating "inoculation is not the cause of every event that occurs within the ten day period [following it].... Without more, this proximate temporal relationship will not support a finding of causation")). While the record in this case establishes that N.A.C. developed PANS between 24-30 hours after vaccination, this fact alone does not provide preponderant evidence that such a short temporal interval is medically appropriate. Petitioner has not met her burden to provide preponderant evidence with respect to *Althen* prong 3.

VIII. Conclusion

Petitioner's desire to understand the abrupt onset of her son's condition is understandable. Equally understandable is her belief that N.A.C.'s vaccinations caused him to develop PANS, due to their temporal proximity to the onset of his illness. However, upon careful evaluation of all the evidence submitted in this matter, including the medical records, the testimony, as well as the experts' opinions and medical literature, I conclude that Petitioner has not shown by preponderant evidence that she is entitled to compensation under the Vaccine Act. **Her petition is therefore DISMISSED. The clerk shall enter judgment accordingly.**[22]

IT IS SO ORDERED.

s/ Katherine E. Oler
Katherine E. Oler
Special Master

[22] Pursuant to Vaccine Rule 11(a), the parties may expedite entry of judgment by each filing (either jointly or separately) a notice renouncing their right to seek review.